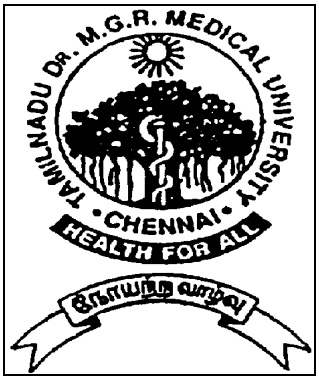
HISTOMORPHOLOGICAL CHARACTERIZATION OF ADULT RENAL NEOPLASMS

Dissertation submitted in partial fulfillment of the requirements for the degree of

M.D. (Pathology) – Branch III



THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI

MARCH 2007

CERTIFICATE

This is to certify that this dissertation entitled **"HISTOMORPHOLOGICAL CHARACTERIZATION OF ADULT RENAL NEOPLASMS"** is a bonafide work done by **Dr.M.SURESH**, in partial fulfillment of the requirements of The TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY, Chennai for the award of M.D. Pathology Degree.

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DECLARATION

I declare that this dissertation entitled **"HISTOMORPHOLOGICAL CHARACTERIZATION OF ADULT RENAL NEOPLASMS"** has been done by me under the guidance and supervision of **Prof.Dr.N.SHANTHI VIJAYALAKSHMI, M.D.,** It is submitted in partial fulfillment of the requirements for the award of the M.D., Pathology degree by The Tamilnadu Dr.M.G.R. Medical University, Chennai. This has not been submitted by me for the award of any degree or diploma from any other University.

Dr.M. SURESH

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I shall be failing in my duty if I do not remember the patients, whose unfortunate illness and diseases have provided me the opportunity to study their pathology.

CONTENTS

INTRODUCTION

Adult renal tumors comprise of neoplasms originating from renal tubular epithelium, urothelium of pelvis, mesenchymal tumors and mixed type of tumors. Among these, renal cell carcinomas (RCC) form the largest group. Over the recent years, there has been approximately 3% annual increase world wide[1] in the age adjusted incidence of renal cell carcinoma. RCC is actually a group of cancers, each with a common cellular origin, distinct genetic abnormalities and unique morphological features.

A number of risk factors – cigarette smoking elevated Body Mass Index, hypertension, having a first degree relative with kidney cancer, End stage Renal Disease[2] have been identified RCC is known to occur sporadically as well as part of inherited cancer syndromes like Von Hippel Lindau Syndrome, Hereditary papillary RCC, Birt Hogg Dube syndrome, Hereditary leiomyoma RCC[3].

The clinical presentation and management of RCC are changing very rapidly, driven by advances in medical imaging, genetics, molecular pathology, surgery, immunotherapy and targeted therapy.

The clinical outcomes of the various histological subtypes are different and accurate histological classification needs attention to gross features, architectural and cytological characteristics with support from histochemical, immunohistological and cytogenetic studies.

Transitional cell carcinoma (TCC) of renal pelvis contributes to a significant proportion of adult renal neoplasms. They are essentially similar to TCC arising in the ureter / urinary bladder.

Oncocyloma and Papillary adenoma are benign renal epithelial neoplasms that have to be differentiated from renal cell carcinoma and can be cured by nephrectomy alone.

Angiomyolipoma is the most common mesenchymal tumor of kidney and was previously considered to be a hamartoma. It has recently been proposed that the periepitheloid cell[4] is the cell of origin. Although the diagnosis of angiomyolipoma is usually straight forward, some cases may show unusual morphological features that may sometimes lead to erroneous diagnosis of malignancy.

AIMS OF THIS STUDY

1. To record the frequency of adult renal neoplasms, particularly RCC among surgical pathology specimens at our Institution.

2. To study the pathological characteristics of these neoplasms and subtype them according to established classification systems.

3. To evaluate the conventional morphological prognostic parameters among the various histological subtypes.

4. To compare the histomorphological profile of these cases with those reported in literature.

REVIEW OF LITERATURE

Renal neoplasms found their way into medical records as early as 1826 with Konig's accurate gross description of kidney tumors[5] and histological studies by Robin (1855) and Waldeyer (1867). They were presumed to arise from proliferation of renal tubular epithelium which later invade the membrana propia and result in a nodular growth.

Grawitz observed the gross and microscopic resemblance of the tumor with adrenal tissue and suggested an origin from adrenal rests within the kidney and coined the term, 'struma lipomatodes aberrata renis'.

In the late 19th century, Doderlein and Birsch Hirschfeld conceived the term hypernephroma. Oberling et al[5] laid to rest the controversy regarding the origin of RCC by providing conclusive electron microscopic (EM) evidence of its origin from renal tubular epithelium. However, recent immunohistochemical findings suggest that they may develop from proximal convoluted tubule (PCT) and collecting duct (CD).

EPIDEMIOLOGY :

The incidence of kidney cancer is considerably higher in developed countries than in developing countries. It affects 1 – 3% of all cancer patients. According to the world cancer report[6], 189000 new cancers are being diagnosed worldwide each year.

The sex ratio is 1.6 to 2:1 in favour of men and most cases occur between 50 and 70 years of age. Kidney cancer causes the death of more than 91000 people each year.

Although the incidence is lesser in Indians when compared to western society, it appears to be steadily increasing. According to the Population Based Cancer Registry[7] maintained at Cancer Institute (WIA), Chennai, the proportion of kidney cancer among all malignancies during 1984 – 93 was 0.66% in males and 0.23% for females. The same figures rose to 1.22% for males and 0.53% for females during 1999 – 2000.

ETIOLOGY :

Numerous agents are known to be associated with development of renal cell carcinoma. (McLaughlin and Lipworth, 2000). The association with smoking was first established as causative for TCC of bladder and has now been extended to RCC[2]. An increased risk of RCC has been liked to obesity and diuretic therapy, particularly in women. The influence of beverages, in particular coffee and alcohol has not been clearly determined despite many studies.

Patients with kidney damage secondary to phenacetin containing analgesic abuse, have an increased risk of TCC. VHL, an autosomal dominant condition is a predisposing factor. Long term hemodialysis used in the treatment of chronic renal disease leads to an increased incidence of acquired cystic disease, which in turn leads to increased risk of RCC.

ETIOLOGICAL FACTORS :

RCC :

- Cigarette smoking
- Germline mutations
- Obesity (in women)
- Hemodialysis (long term)
- Hypertension
- Sickle cell trait.

UROTHELIAL CARCINOMA OF RENAL PELVIS

- Cigarette smoking
- Phenacetin abuse
- Thorium exposure
- Balkan nephropathy
- Urothelial tumor of urinary bladder

EVOLUTION OF CLASSIFICATION AND STAGING SYSTEMS

The earliest known classification system was devised by Konig based on gross morphology – fungoid, medullary, scirrhous, steatomatous types.

According to microscopic appearance, RCC was initially grouped into four main histological types – clear cell, granular cell, tubulopapillary and sarcomatoid. Later as a result of greater sophistication in tumor analyses (histochemistry, EM of microvesides, 1HC of mtermediate filaments),

many other distinct types were suggested which resulted in the Mainz classification.

This system recognised clear cell, chromophobe, chromophil, spindle shaped, oncocytic and unclassified types.

In the 1990s, advances in the understanding of genetic alterations in RCC reinforced the concept that there were distinct subtypes of RCC, each with its own genetic lesions. Different genetic alterations affect cellular biology differently, leading to different tumor morphology and behaviour.

The Heidelberg classification[8] (1996) sought to integrate these genetic lesions with readily recognizable histological types – conventional, papillary, chromophobe, collecting duct and unclassified types (Kovacs et al 1997).

In 1997, UICC and AJCC[9] released their combined workgroup classification of RCC. This was based on Mainz classification but like Heidelberg workshop, took into consideration and integrated morphology with genetic features.

UICC/ AJCC (Storkel et al, 1997)

BENIGN :

- Papillary adenoma
- Renal oncocytoma
- Metanephric adenoma
- Metarephic adenofibroma

MALIGNANT :

Conventional (clear) cell RCC

Papillary RCC

Chromophobe RCC

Collecting duct carcinoma

Unclassified RCC

CLASSIFICATION OF RENAL TUMORS IN ADULTS (WHO 2004)

RENAL EPITHELIAL TUMORS

BENIGN

Renal oncocytoma
Papillary adenoma
Metanephric adenoma
Metanephric adenofibroma

MALIGNANT

Clear cell (conventional) RCC
Papillary RCC
Chromophobe RCC
Collecting duct carcinoma
Medullary carcinoma
Mucunous tubular and spindle cell carcinoma
XpII translocation carcinoma
Renal cell carcinoma, unclassified

TUMORS OF UNDETERMINED MALIGNANT POTENTIAL

Multilocular cystic RCC

MIXED EPITHELIAL AND STROMAL TUMORS

Mixed epithelial and stromal tumor

Cystic nephroma

NON EPITHELIAL TUMOURS

BENIGN

Renomedullary interstitial cell tumor

Angiomyolipoma

Juxta glomerular cell tumor

Metanephric stromal tumor

Solitary fibrous tumor

Lipoma

Leiomyoma

Hemangioma

Lymphangioma

MALIGNANT

Leiomyosarcoma

Rhabdomyosarcoma

Synovial sarcoma

Liposarcoma

MISCELLANEOUS TUMORS

Carcinoid tumor

PNET

Small cell carcinoma

Metastatic tumors

Hematopoietic tumors

Unclassified RCC remains as a diagnostic category for tumors that do not adequately fulfill the criteria for all other categories.

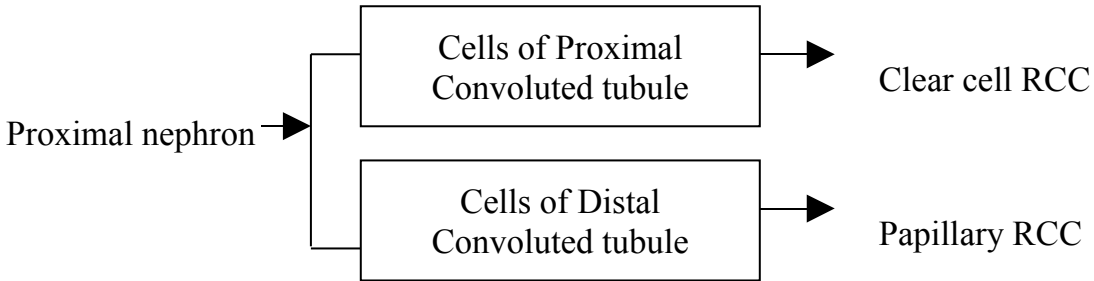
Sarcomatoid and granular categories have been removed from current RCC tumor classification schemes because these terms are no longer considered useful. Sarcomatoid RCC is not a distinct histological entity and represents high grade transformation in different subtypes of RCC[10]. Granular cells have been found in almost all subtypes in varying proportions.

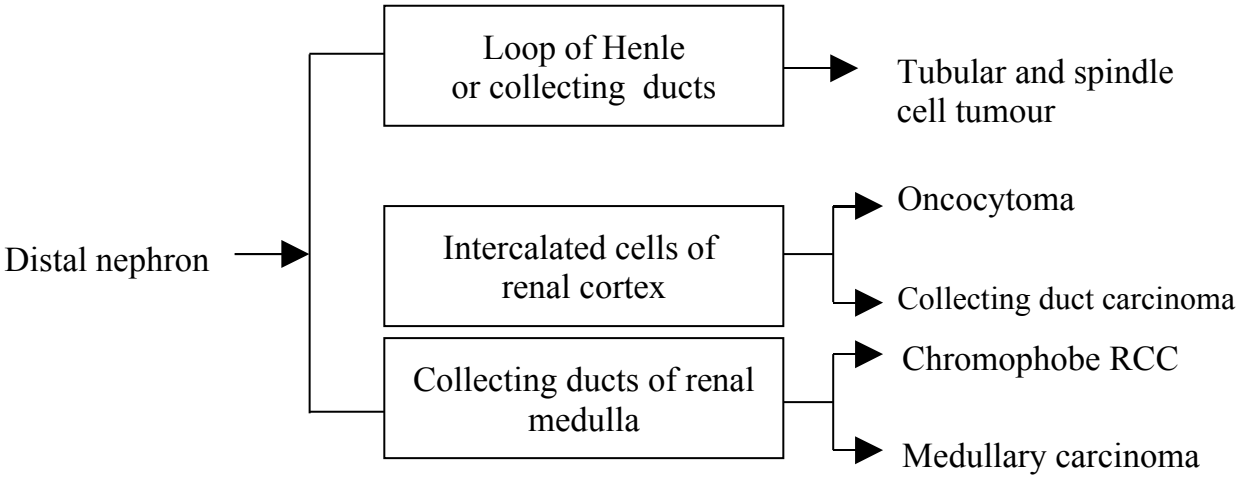
A variant of clear cell RCC with predominantly cystic pattern called as multilocular cystic RCC is thought to have low potential for recurrence or metastasis. Papillary RCC is divided into type I and type II based on the cells lining the papillae.

Chromophobe RCC has been proposed to originate in the intercalated cells of the renal collecting ducts and there is a high proportion of low stage tumors at presentation.

Collecting duct carcinoma or Bellini duct carcinoma, an aggressive RCC variant, appearing to arise in medullary collecting ducts. Renal medullary carcinoma is a newly described variant of the collecting duct type which occurs almost exclusively in African – American men with sickle cell trait or sickle cell disease.

Cell of Origin of Renal tumors[11]





RCC is now recognised as a family of cancers that results from distinct genetic abnormalities with unique morphological features but all derived from renal tubular epithelium. Conditions that may be complicated by RCC are VHL, acquired cystic disease, adult form of polycystic kidney disease, Tuberous Sclerosis, Neuroblastoma, familial cutaneous leiomyomatosis, malignant lymphoma.

The tumor is usually centred at the cortex, grows asymmetrically, extending towards the renal capsule and also towards the pelvis. The renal sinus is the compartment of fatty tissue located within the confines of the kidney that envelopes the collecting system. The absence of a fibrous barrier between the renal sinus and the renal cortex enables easy access to vascular structures in the sinus. In this way, the tumor may invade the renal vein,

inferior vena cava and can even extend into the right atrium. Renal sinus invasion is the most common site of extra renal extension of renal carcinoma.

Approximately one – third of patients with RCC already have distant metastasis[12] at the time of presentation. Common sites of metastasis are lungs and bones, mainly pelvis and femur. RCC can metastasize to unusual sites with a silent primary and hence can be confused with primary tumor in the organs in which they lodge.

The light microscopic features for subtyping RCC are fairly well defined by the WHO. The ultrastructural feature studied by electron microscopy lends additional support to the current classification schemes and provides insights into possible histiogenesis of renal epithelial neoplasms[13]. Clear cell RCC showed long microvilli with abundant cytoplasmic lipid and glycogen. Papillary RCC showed variably sized microvilli and small amount of cytoplasmic lipid and glycogen. Papillary RCC showed variably sized microvilli and small amount of cytoplasmic lipid but no glycogen. Chromophobe RCC showed many cytoplasmic vesicles and abnormal mitochondria with rare short and stubby microvilli. Renal oncocytoma showed many mitochondria with few vesicles.

IMMUNOHISTOCHEMISTRY :

The diagnosis of primary or metastatic RCC can be difficult especially in small biopsies because of the wide variety of histological appearance and clinical presentation that RCC can assume. All RCCs stain positive with

cytokeratin cocktail (AE_1/AE_3 and CAM 5.2), LMW CK and EMA. Clear cell and papillary variants also stain with vimentin whereas chromophobe variant does not stain with vimentin. Collecting duct carcinoma has a unique staining pattern, reacting with both low and high molecular weight cytokeratin, peanut agglutinin, Ulex europeus and EMA similar to distal collecting duct and tubular epithelium.

MOLECULAR GENETIC FEATURES :

Sporadic clear cell RCC typically show 3p deletion in the region harbouring VHL gene. Sporadic papillary RCC is characterised by trisomies especially of 7, 17 and loss of Y. Chromophobe RCC is characterised by combined losses of multiple chromosomes 1, 2, 6, 10, etc.

GENETIC LESIONS IN RENAL TUMOURS:

Clear cell RCC	loss of 3p mutations/hypermethylations of VHL gene
Papillary RCC	trisomies of 7 and 17 loss of chromosome Y MET mutation in familial cases
Chromophobe RCC	hypodiploidy loss of chromosomes 1,Y,6,10,13
Renal oncocytoma	loss of chromosome Y t(9:12) (p23:q13) t(5:11) (q35:q13)
Collecting duct carcinoma	monosomies of 1,6,14,15,22 loss of heterozygosity of 1q
Xp11 translocation carcinoma	t(x:1) (p11.2:q21) t(x:17) (p11.2:q25)
Mucinous tubular and spindle cell carcinoma	loss of chromosomes 1,4q,6,8p
Angiomyolipoma	TSC 1 and TSC 2 gene activation
Metanephric adenoma	loss of 2p

The classic diagnostic triad of clinical symptoms – hematuria, flank pain, abdominal mass is found only in a minority of patients. Other symptoms are weight loss, anemia, fever and those due to metastasis, paraneoplastic syndromes like hypercalcemia, leukemoid reaction, systemic amylodosis etc.

Many pathological features were found to correlate with tumor behaviour[14]. These include tumor staging, Fuhrman's nuclear grading, histological subtype, sarcomatoid change, amount of necrosis, markers of tumor proliferation, metastasis etc. However, the search for new molecular prognostic markers has proved elusive over the years[15].

Tumor stage, which reflects the anatomic spread and involvement of disease, is recognised as the most important prognostic indicator for clinical behaviour and outcome of RCC. Currently, Robsons staging and TNM staging systems (revised in 1997) are in use.

Robsons Staging of RCC

Stage I	:	Tumor confined by renal capsule
Stage II	:	Tumor extension to perirenal fat or ipsilateral adrenal but confined by Gerota's fascia
Stage III a	:	Tumor involvement of renal vein or IVC
Stage III b	:	Lymphatic involvement
Stage III c	:	Veins and lymphatic involvement
Stage IV a	:	Spread to contiguous organs except ipsilateral adrenal
Stage IV b	:	Distant metastasis

TNM Staging of RCC

PRIMARY TUMOR (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7cm or less in greatest dimension, limited to kidney
T1a	Tumor 4cm or less in greatest dimension, limited to kidney
T1b	Tumor more than 4cm but less than 7cm in greatest dimension, limited to kidney
T2	Tumor more than 7cm in greatest dimension, limited to kidney
T3	Tumor extends into major veins or invades adrenal gland or perinephric tissue but not beyond Geroter's fascia
T3a	Tumor directly invades adrenal gland or perirenal and/ or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor grossly extends into the renal vein or its segmental branches or IVC below diaphragm

b

T Tumor grossly extends into vena cava above diaphragm or invades the wall

3 of vena cava

c

T Tumor invades beyond Gerota’s fascia

4

Regional Lymph Nodes (N)

N Regional lymph nodes cannot be assessed

X

N No regional lymph node metastasis

0

N Metastasis in a single regional lymph node

1

N Metastasis in more than one regional lymph node

2

Distant Metastasis

M Distant Metastasis cannot be

X assessed

M No distant metastasis

0

M Distant Metastasis

Numerous grading systems have been developed for RCC. Skinner[16] and associates in 1971 were the first to propose a grading system based on nuclear morphology alone. Fuhrman and colleagues simplified this system in 1982. This method is widely in use today. Histologic tumor necrosis, if > 50% has been shown to reflect the rate of progression of tumors[17].

The recently recommended histological classification and revised TNM staging have allowed identification of prognostic groups among patients with RCC.

Holger Moch and Mahul B. Amin et al[18] studied the prognostic utility of revised TNM staging systems in 588 renal cancers. In their analysis the new TNM stage strongly correlated with patient survival.

Although molecular analyses have revealed genetic differences between morphologic tumor entities, the prognostic significance of histological tumor types is controversial. Published literature shows conflicting information regarding behaviour of tumor among different genetic categories[19].

Recent reports have discounted differences in presentation, morphological features as well as patient outcome among histological subtypes of RCC. One study found that patients with clear cell RCC were more likely to present with advanced stage and symptoms compared with

patients with papillary and chromophobe RCC. In addition, 23% of patients with papillary RCC were multifocal compared with only 7% and 8% of patients with clear cell and chromophobe RCC respectively. Cancer specific survival rates at 5 years following surgery for patients with chromophobe, papillary and clear cell RCC were 100%, 86% and 76% respectively.

Moch et al, in a similar study of RCC from swiss patients, found that patients with chromophobe RCC had significantly improved prognosis compared with those of clear cell RCC (5 year survival rates of 78% and 50%). They did not find significant differences in outcome between patients with chromophobe and papillary RCC or between patients with clear cell and papillary RCC.

John C. Cheville et al[21], at the Mayo clinic, compared cancer specific survival rates and examined association of outcomes with histological subtypes and demonstrated significant differences, highlighting the need for accurate subtyping.

Mahul B. Amin, after studying 405 cases at the Henry Ford Hospital[20], concluded that the clinical outcome of various histological subtypes are different. These studies lent support to the morphological and the reported cytogenetic – molecular distinctiveness of subtypes of renal epithelial tumors.

Arnaud Mejean, in a review article[14], has concluded that the most useful prognostic factors of RCC were TNM stage, histological grade, subtype, performance status, patient's age, metastasis and time to appearance of

metastasis. Various other studies have attempted to evaluate prognostic factors for patient survival in different subtypes of RCC.

TCC of renal pelvis usually occurs in adults. It may be seen in association with analgesic abuse, thorotrast administration and cyclophosphamide therapy. It usually presents with hematuria without a palpable mass. Synchronous or metachronous tumors occur very commonly (40%). They have a tendency to implant along the ureter and hence it is important to resect the bladder cuff.

STAGING SYSTEM FOR TCC OF RENAL PELVIS

T Non invasive papillary carcinoma

0

T TCC in situ

i

s

T Invasion of lamina propria

1

T Invasion of muscularis propria

2

T Extension into peripelvic fat or renal parenchyma

3

T Invasion of adjacent organs or extension through kidney into perirenal

4 fat

N Metastasis in single node < 20 mm

1

N Metastasis in single node > 20 mm and < 50 mm

2 Or multiple nodes each < 50 mm

N Nodal metastasis > 50 mm

3

M Distant metastasis

1

Other carcinomas like squamous cell carcinoma, lymphoepithelioma like carcinoma, carcinosarcoma, small cell neuroendocrine carcinoma occur very infrequently.

Angiomyolipoma is a mesenchymal tumor composed of an intimate admixture of vessels, smooth muscle and fat. It can occur as a component of tuberous sclerosis complex. Usually the morphology is characteristic on hematoxylin and Eosin sections but immunostains may be needed in diagnosing unusual cases. There is coexpression of muscle markers – SMA and muscle specific actin and markers of melaninogenesis like HMB 45.

Hormonal receptors are also positive in many cases[22]. Rarely malignant transformation has been reported[23].

MATERIALS AND METHODS

PATIENT SELECTION :

The surgical specimens and pathology reports of patients who underwent radical nephrectomy for renal tumours during the period January 2003 to June 2006 at the Institute of Pathology, Madras Medical College, formed the material for this study. Consultation slides received for institutional review were also included. Patients who were below 18 years of age and those who lacked details of important pathological features, were excluded from the study.

CLINICAL FEATURES :

The clinical features such as age, sex of the patient, laterality of the tumour, and type of surgery were noted from the clinical case sheets.

GROSS MORPHOLOGY :

The gross characteristics of the tumour included the tumour location, size, necrotic, areas, capsular invasion, vascular and ureter invasion were evaluated. These details were collected directly from the specimens or obtained from the pathology report registers.

The specimens were fixed in 10% formalin. After adequate fixation, gross examination was done according to protocol. Tissue bits were taken as were deemed necessary and embedded in paraffin. Sections were cut using rotary microtome. The section were stained routinely with hematoxylin and

Eosin. Special stains like Hale's colloided iron were employed as and when required.

HALE'S DIALYSED IRON STAIN[24]

1. Dewax a positive control and test section and bring to distilled water
2. Treat all sections with equal parts of dialysed iron and acetic acid, 10 min
3. Wash well in several changes of distilled water.
4. Treat with filtered Perls' reagent, 10 min
5. Wash well in several changes of distilled water
6. Counterstain with 0.5% aqueous neutral red, 5 min
7. Wash in water
8. Rinse in absolute alcohol
9. Clear in xylene and mount in a DPX – type mountant

MICROSCOPIC FEATURES :

The microscopic features were assessed after reviewing all the available slides. These included the histological subtype, nuclear grade, histological tumour necrosis, presence of sarcomatoid component, capsular invasion, renal sinus invasion and ureteric invasion.

Histological subtying was done accoding to UICC/AJCC and Heidelberg classification guidelines.

DEFINITIONS :

The working definitions used in this study are as follows

Clear cell RCC were defined[18] by a solid, acinar or cystic growth pattern and by predominance of cells with clear cytoplasm in routine sections, although large foci with eosinophilic cells were also common.

Chromophobe RCC[18] had a solid, alveolar or nested architecture and an eosinophilic or pale cytoplasm. These tumours stained with Hale's colloidal iron, showed diffuse and strong reticular positivity.

A tumour was considered papillary RCC[18] if a papillary architecture predominated and no solid clear cell areas were present. Papillary tumours were divided into basophilic (type 1) and eosinophilic (type 2) according to the prominent cell type according to the recommendations of Delahunt, Eble and Amin et al. In type 1 tumours, the papillae were covered by cells with scanty cytoplasm, small oval nuclei with inconspicuous nucleoli, foamy macrophages in papillary cores and psammoma bodies. The papillae of type 2 tumours were covered by large cells with abundant eosinophilic cytoplasm and large nuclei with prominent nucleoli.

Collecting duct carcinoma was diagnosed if there were irregular channels lined by highly atypical epithelium and desmoplastic stroma.

Tumour was diagnosed as renal oncocytoma if the characteristic architectural (nested, tubulocystic, mixed), cytoplasmic (eosinophilic finely

granular cytoplasm) and nuclear features (round nuclei with uniform chromatin distribution with or without prominent nucleoli) were present.

The term renal capsule[25] was used to refer to the connective tissue layer that envelops the kidney along its external surface and extends slightly into the hilum.

Capsular invasion was defined[25] as either tumour cells within vascular structures that are clearly within the perinephric fat or tumour cells in direct contact with perinephric stroma or fat cells without a connective tissue layer of separation.

The renal sinus[25] referred to the central fatty compartment that invests the collecting system and abuts the cortical columns of bertini without a connective tissue interface.

Sinus invasion[25] is defined as either tumour within vascular structures that are clearly within the renal sinus fat or tumour cells in direct contact with renal sinus stroma or fat cells.

In transitional cells carcinoma the microscopic architecture was variable – nests, small clusters, ribbons and diffuse. The neoplastic cells were usually of medium size with moderate amount of cytoplasm. The degree of nuclear atypia was noted. Invasion into lamina propria, muscularis propria, peripelvic fat and renal parenchyma were looked for. The presence of necrosis, mitotic activity and inflammation were also recorded.

The diagnosis of angiomyolipoma required an intimate admixture of fat, smooth muscle and blood vessels in varying proportions.

GRADING :

Nuclear grade for clear cell RCC was determined using standard criteria[16]. (Fuhrman)

Grade	Nucleus	Nucleolus
1	Round, uniform, 10μ diameter	Inconspicuous or absent
2	Slightly irregular, 15 μ diameter	Visible at x 400
3	Very irregular, 20 μ diameter	Visible at x 100
4	Bizarre multilobated, 20μ diameter with clumped chromatin	Prominent

The highest grade occupying at least one high power field (HPF) was assigned to the tumour, in accordance with the criteria of Fuhrman et al.

In papillary RCC, type 1 tumours were given a nuclear grade I/II and type 2 tumours were given a nuclear grade III/IV.

Chromophobe RCC tumours were not given nuclear grade because of their uniformly indolent behaviour.

The presence of a sarcomatoid component in any type of RCC was recorded. By definition all tumours with a sarcomatoid component were assigned grade IV.

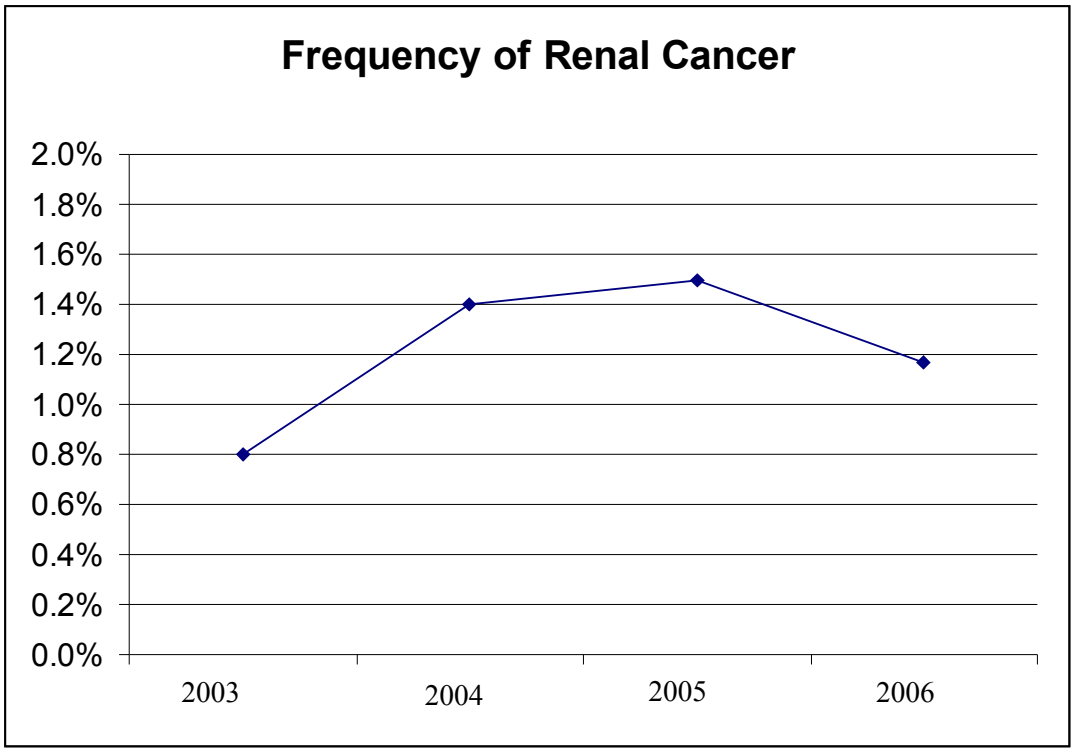
Histologic tumour necrosis was defined[21] as the presence of any microscopic coagulative necrosis. Degenerative changes such as hyalinization, hemorrhage and fibrosis were not considerd necrosis. The amount of necrosis as a percentage was quantified into 3 groups, 0-25%, 25-50% and 50-100%.

STATISTICAL ANALYSIS :

The significance of differences in the pathological features among different histologic subtypes were tested using Chi – square (χ^2) test[26]. 95% confidence limits were set and a difference in the parameters was regarded as significant when $P < 0.05$.

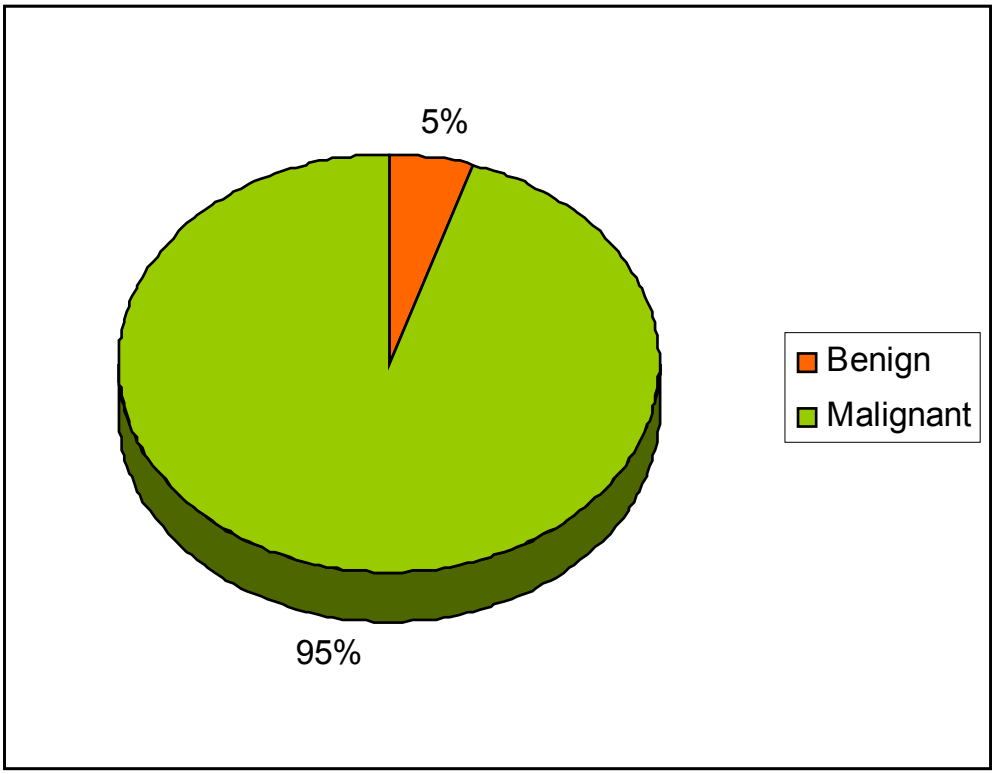
DATA ANALYSIS

In our study, 79 renal tumours, were obtained during the period January 2003 to June 2006. There were 21 cases during 2003, 25 cases during 2004, 19 cases during 2005 and 14 cases in 2006 upto June. The proportion of renal cancers among all cancers diagnosed at the department of pathology, MMC during the years were 0.8%, 1.4%, 1.5% and 1.17% respectively.

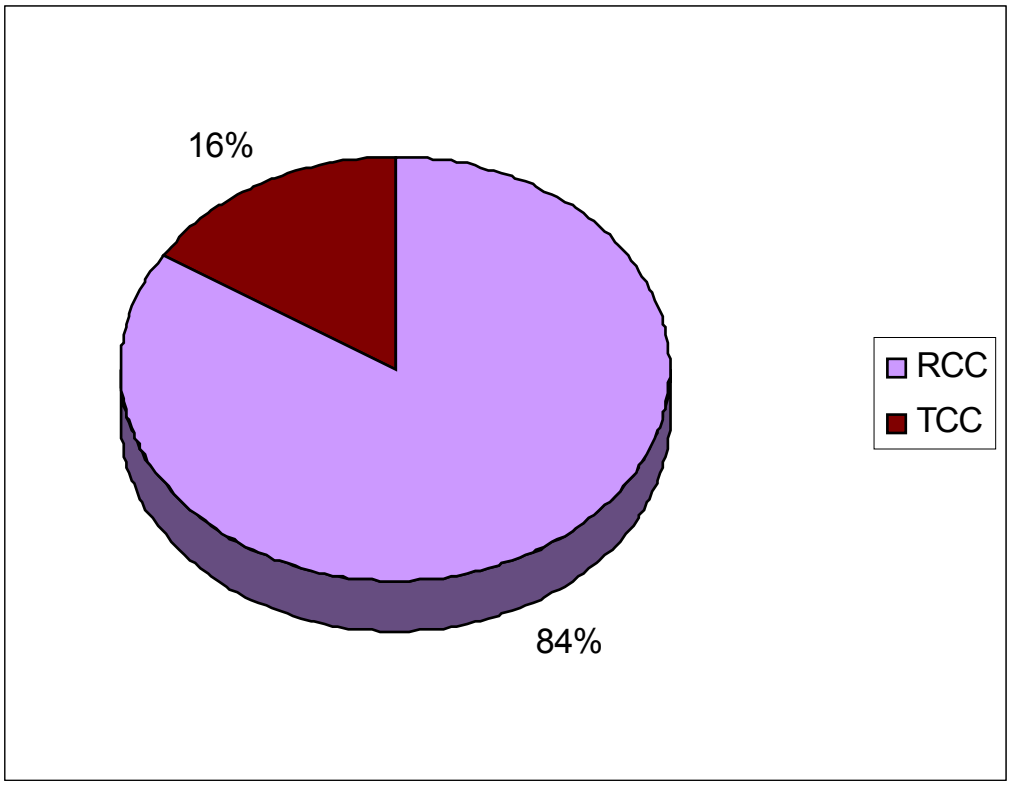


Out of 79 renal tumours studied, 75 (95%) were malignant and 4 (5%) were benign. Among the malignant tumours, 63 (84%) were RCC and 12 (16%) were TCC.

RENAL TUMOURS



MALIGNANT TUMOURS

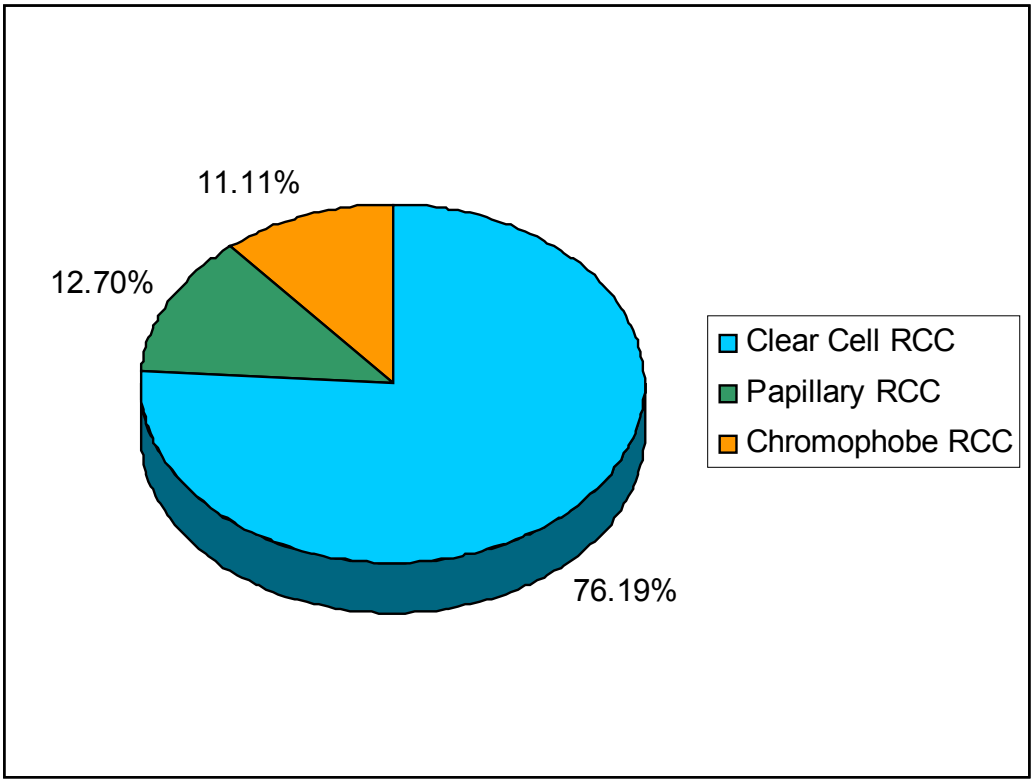


The various subtypes of RCC were distributed as follows :

Table 1 :

Subtype	Number	Percentage
Clear cell RCC	48	76.19%
Papillary RCC	8	12.70%
Chromophobe RCC	7	11.11%

RCC SUBTYPES



AGE DISTRIBUTION AND SEX RATIO

The age of patients ranged from 22 years to 80 years with a mean of 52.61 years. The mean age for benign tumours was 42.50 years and that for malignancies was 53.74 years.

Table 2 :

Tumour	Age		Sex Ratio (M : F)
	Mean (yrs)	Range (yrs)	
RCC	54.03	22 – 80	2.7 : 1
TCC	53	32 – 75	5 : 1
Angiomyolipoma	41.67	22 – 55	1 : 2
Hemangioma	45	-	-

The age wise distribution and sex ratio of the different subtypes of RCC are as follows :

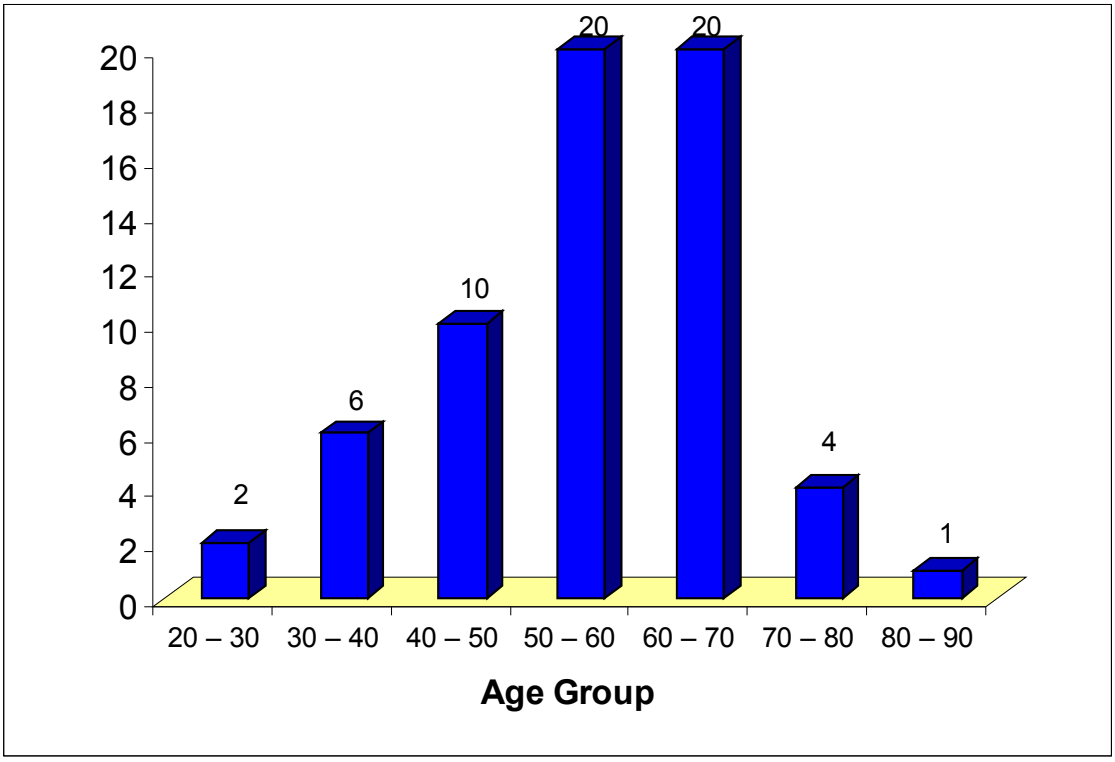
Table 3:

Subtype	Age		Sex Ratio (M : F)
	Mean (yrs)	Range (yrs)	
Clear cell RCC	55.57	22 – 80	3.4 : 1
Chromphobe RCC	44.14	30 – 55	1.3 : 1
Papillary RCC	52.13	35 – 70	1.7 : 1

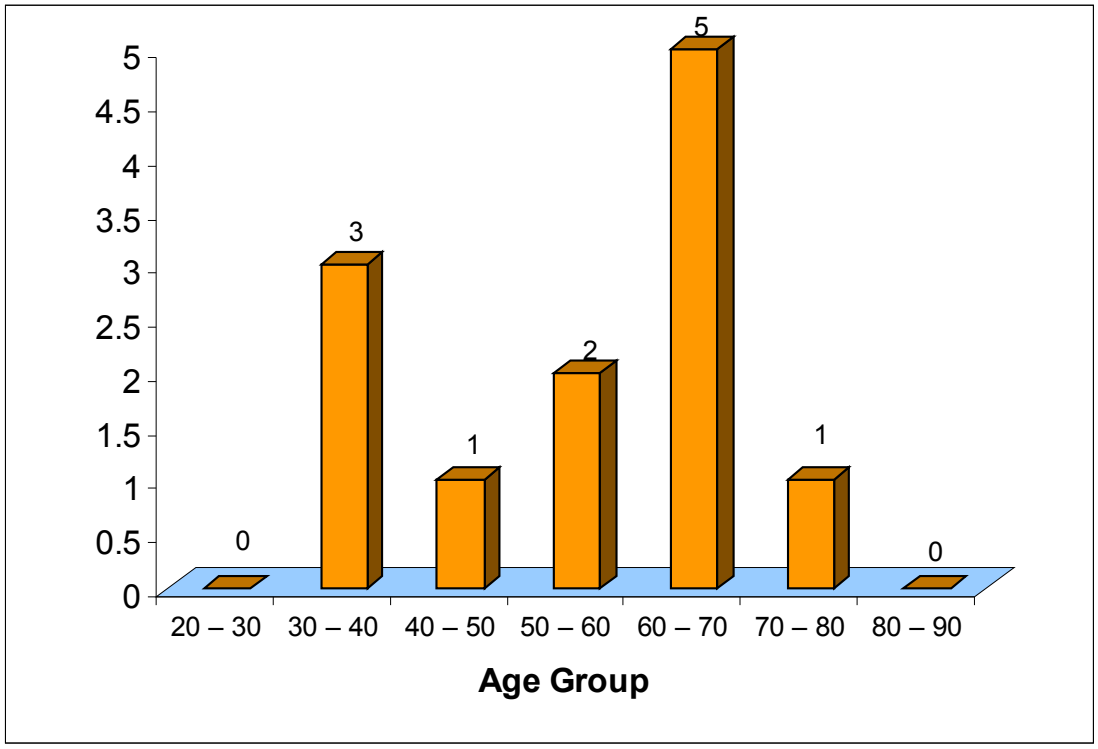
Table 4 :

Age group (yrs)	RCC	TCC	Benign Neoplasm
20 – 30	2	0	1
30 – 40	6	3	0
40 – 50	10	1	2
50 – 60	20	2	1
60 – 70	20	5	0
70 – 80	4	1	0
80 – 90	1	0	0
Total	63	12	4

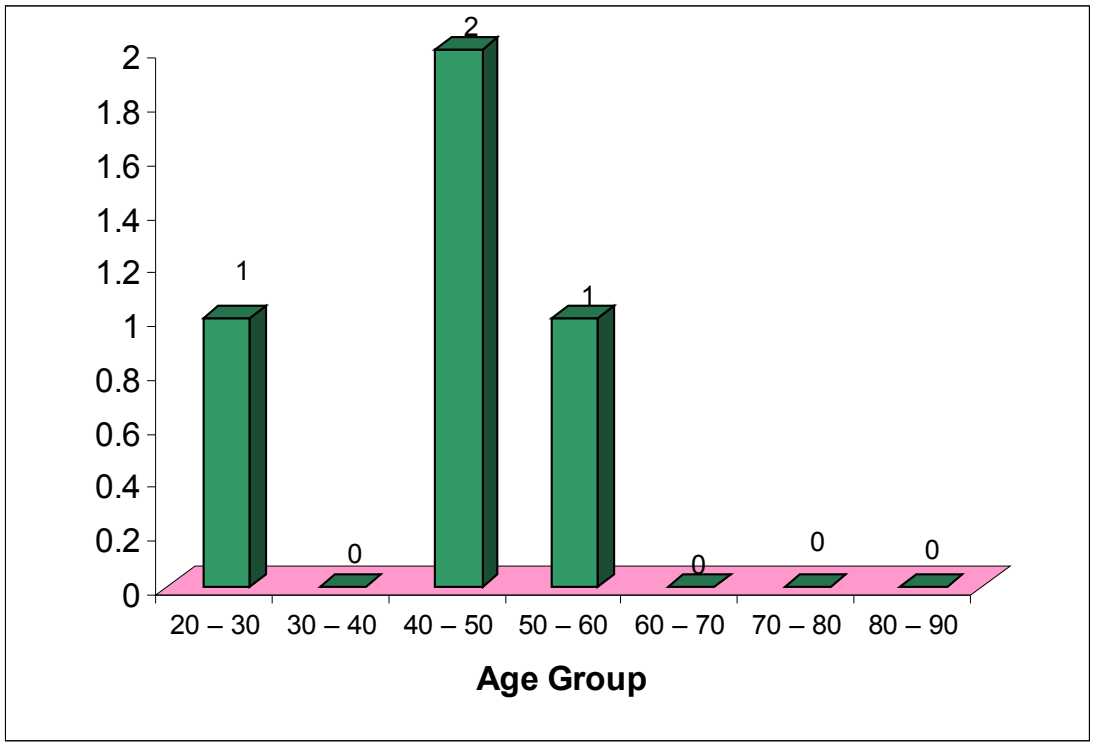
HISTOGRAM SHOWING AGE- SPECIFIC FREQUENCY OF RENAL TUMOURS - RCC



HISTOGRAM SHOWING AGE- SPECIFIC FREQUENCY OF RENAL TUMOURS - TCC



HISTOGRAM SHOWING AGE- SPECIFIC FREQUENCY OF RENAL TUMOURS – BENIGN TUMOURS



LATERILITY :

Malignant tumours had a slight predilection for left kidney (1.1 : 1) whereas benign tumours occurred on each side with equal frequency. There were no bilateral tumours. Multifocality was noted in three cases of TCC.

SIZE OF TUMOUR :

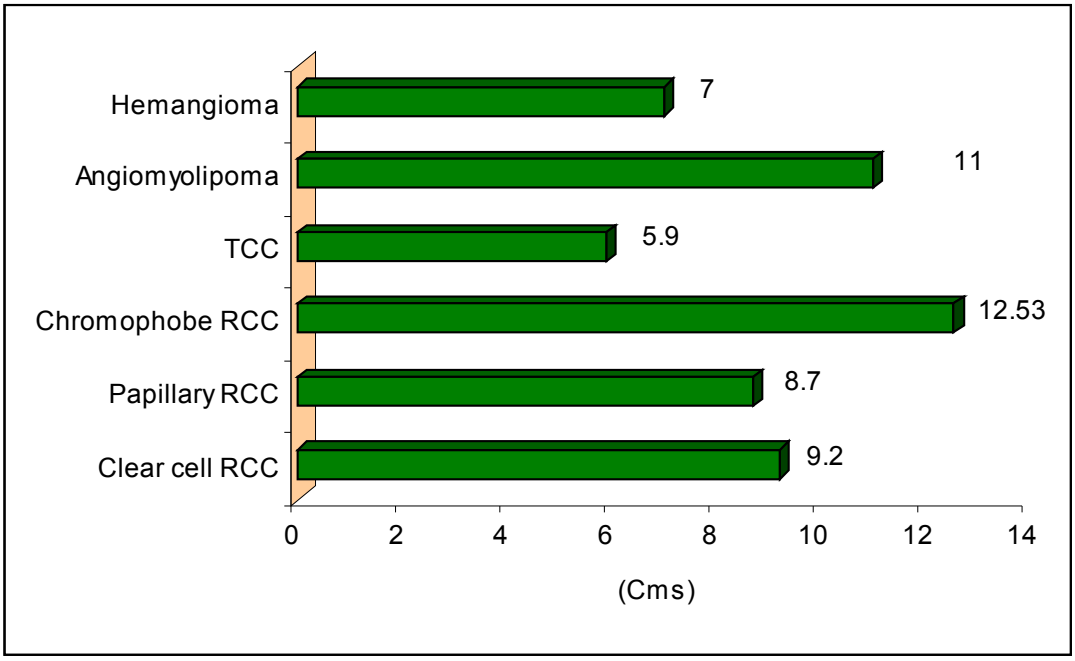
The size of the tumour was taken as its greatest dimension. It ranged from 2 cm to 20 cm. The mean size of each histological subtype is tabulated below.

Table 5 :

Histological type	Size*	
	Mean (cm)	Range (cm)
Clear cell RCC	9.2	4 – 18
Papillary RCC	8.7	5 – 15
Chromophobe RCC	12.53	9 – 20
TCC	5.9	2 – 10
Angiomyolipoma	11	8 -15
Hemangioma	7	-

* Size was not known for 5 cases of clear cell RCC and one case of Papillary RCC

Mean Size of Renal Tumours



Nuclear grading according to the Fuhrman's criteria was done and the following data were obtained.

Table 6 :

Grade	No. of Cases **	Percentage
I	1	2.33
II	15	34.88
III	14	32.56
IV	13	30.23

** Five cases were not assigned nuclear grades as not all their slides were available for review.

Grading in two tier system

Table 7 :

Grade	No. of cases	Percentage
Low	16	37.21
High	27	62.79

The mean size of the tumours under each grade was calculated.

Table 8 :

Grade	Mean size (cm)
I	5.5
II	7.59
III	10.51
IV	10.9

Among papillary RCC, 5 cases were type I and were assigned grade I and 3 cases were type II and were assigned grade II.

When Fuhrman's nuclear grading scheme was applied to 7 cases of chromophobe RCC, 5 were grade II and 2 cases were grade III. All 12 cases of TCC were grade III tumours.

Sarcomatoid components were found in 5 cases of clear cell RCC in varying amounts ranging from 10 to 95%. No other subtypes showed there sarcomatoid changes.

NECROSIS

The amount of tumour necrosis in clear cell RCC tumours was quantified as < 25%, 25 – 50% and > 50%.

Table 9:

Necrosis	No. of cases*
< 25%	19
25 – 50%	17
> 50 %	7

* 5 cases were excluded because they did not have all the slides for quantification of necrosis.

The amount of necrosis, analysed gradewise, is given in the following table.

Table 10:

Grade	Necrosis		
	< 25 %	**25 – 50%**	**> 50%**
I	1	0	0
II	12	3	0
III	4	7	3
IV	2	7	4

In two tier grading system the same data can be tabulated as follows

Table 11:

Grade	Necrosis		
	< 25 %	**25 – 50%**	**> 50%**
Low (I/II)	13	3	0
High (III/IV)	6	14	7

$x^2 = 16.10$ degree of freedom (D.F) =2 $P < 0.001$

The correlation between age, mean size of the tumour, nuclear grade and necrosis was analysed.

Table 12 :

Age group (yrs)	Mean size (cm)	Nuclear grade	Amount of necrosis
0-30	8	II – 50% III – 50%	< 25% - 50% cases > 50% - 50% cases
30 – 50	8.4	II – 33% III – 33% IV – 33%	< 25% - 16% cases 25 – 50% - 84% cases
> 50	9.9	I – 3.2% II – 26.8% III – 43.4% IV – 26.6%	< 25% - 43.2% cases 25 – 50% 33.4% cases > 50% - 13.4 cases

CAPSULAR AND VASCULAR INVASION

The only grade I clear cell RCC did not show either capsular or vascular invasion. Among grade II tumours, 5 cases had capsular invasion only, 6 cases had vascular invasion only and 4 cases had neither.

Among grade III tumours, one cases had capsular invasion, 3 had vascular invasion only and 10 cases showed both.

Out of 13 grade IV tumours, 2 had capsular invasion, 3 had vascular invasion only and 8 cases showed both.

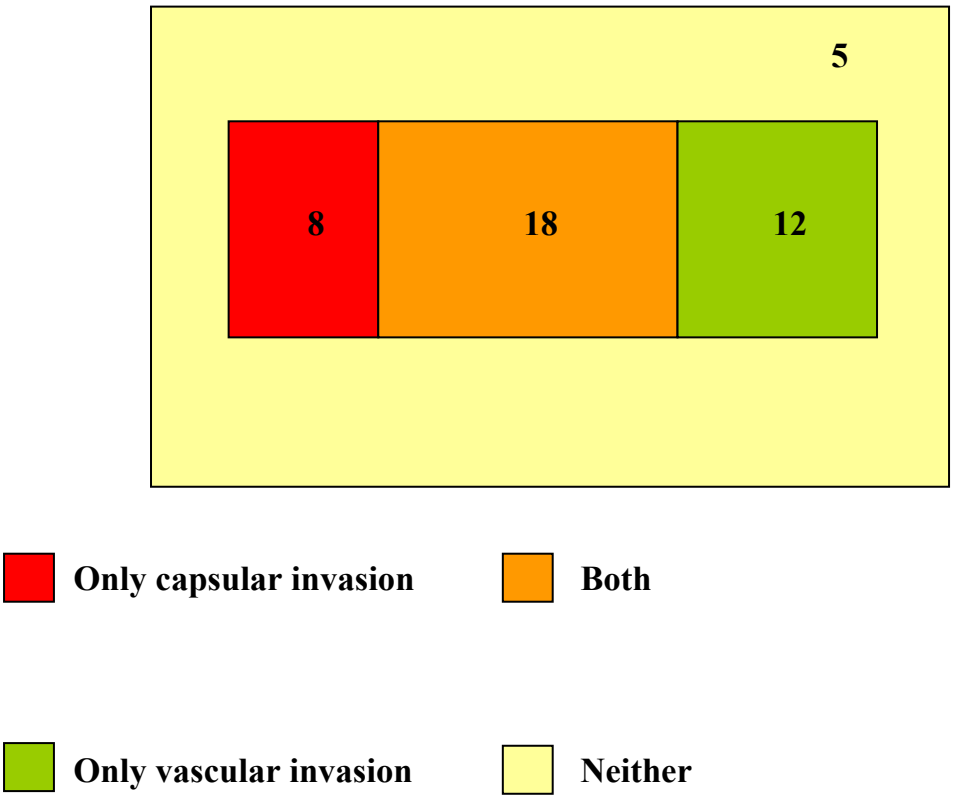


Table 13 :

Grade	Capsular invasion only	Vascular invasion only	Both	Neither
I	-	-	-	1 (100)
II	5 (33.33)	6 (40)	-	4 (26.67)
III	1 (7.14)	3 (21.42)	10 (71.44)	-
IV	2 (15.38)	2 (23.08)	8 (61.52)	-
Total	8	12	18	5

(Figures within brackets indicate percentage of cases)

Table 14 :

Grade	Capsular invasion	No capsular invasion	Total	Rate of invasion
Low	5	11	16	31.25
High	21	6	27	77.78
Total	26	17	43	60.47

$\chi^2 = 9.11$ D.F. = 2 $P < 0.005$

Table 15 :

Grade	Vascular invasion	No vascular invasion	Total	Rate of invasion
Low	6	10	16	37.5%
High	24	3	27	88.89%
Total	30	13	43	69.77%

$\chi^2 = 12.56$ D.F. = 2 $P < 0.001$

Among 12 cases of TCC, 6 cases showed contiguous ureteric invasion.

Angiomyolipoma was diagnosed in three cases. The mean age was 41.67 years with sex ratio 1 : 2 in favour of females . None of the patients had tuberous sclerosis.

A single case of hemangioma in a 45 year F was recorded. It was 7 cm size. Microscopically extensive hemorrhagic areas were seen but no necrosis or atypical features were noted.

DISCUSSION

The number of renal cancers diagnosed in our department shows a definite increase over the preceding three years. While increase in the number of surgeries is also a factor, the increase in proportion of renal cancers among total malignancies suggests that there is a real increase in incidence of renal cancer. This trend is also reflected in the statistics published[7] by the Population Based Cancer Registry (PBCR) at Cancer Institute (WIA), Chennai.

The malignant tumours constituted the vast majority of our cases while benign tumours were very less in number. (95% and 5% respectively). The proportion of malignancies in our study is higher when compared to the figure of 86.7% in a study of 469 nephrectomies at Szeged university[27].

There was a clear male preponderance in case of malignancies (2.9 : 1) which was higher for TCC (5 times) than RCC (2.7 times). This may result from the role of smoking as a causative factor in the pathogenesis of renal cancer.

The age of patients with RCC was distributed in a wide range of 22 to 80 years with peaks in sixth and seventh decades. TCC had a more uniform age distribution. Benign tumours were found in the younger age groups.

Clear cell RCC was the most frequent tumour (76.19%) in our series, followed by papillary RCC (12.7%) and chromophobe RCC (11.11%). These figures are in broad agreement with those reported by Nemeth. I et al[27] (88.4%,

5.6%, 4%) Bonsib et al (70.97%, 16.13%, 12.90%) and the same author in another study (74%, 16%, 7%).

FREQUENCY OF HISTOLOGIC SUBTYPES

Table 16

Histological subtype	Mahul Amin et al[20] n = 377	Holger Moch et al [18] n = 588	Bonsib et al[23] n = 100	John C. Cheville et al[21] n = 2385	Our study n = 63
Clear cell RCC	63%	83%	74%	83.2%	76.19%
Papillary RCC	18.5%	11%	16%	11.3%	12.70%
Chromophobe RCC	5.9%	5%	7%	4.3%	11.11%
Others	5.7%	1%	3%	1.2%	-

All subtypes except papillary RCC showed a preference for left kidney and the male – female ratio was highest for clear cell RCC among all tumours.

The mean size of the tumour was largest for chromophobe RCC (12.53 cm), followed by clear cell RCC (9.2 cm) and papillary RCC (8.7cm). some authors contend that the chromophobe RCC are slow growing tumours and hence present with symptoms only after reaching a considerably large size.

In the study by Igor Frank et al[28], the mean tumour sizes for clear cell RCC, papillary RCC and chromophobe RCC were 6.5cm, 4.7cm and 7.9cm respectively. This study was conducted in the western population where

patients present early for diagnosis and many tumours are diagnosed on imaging performed for other complaints.

Our study showed good correlation of size of the tumour with age. In the 0 – 30 years age group, the mean size was 8 cm. The mean size increased to 8.4cm for 30 – 50 yrs and 9.9cm for > 50 years age group. Presumably, the older age group patients present with a higher stage due to this reason.

A summary of the nuclear grading of clear cell RCC is given table 6. only one patient presented with grade I whereas there were fifteen patients with grade II, fourteen patients with grade III and thirteen patients with grade IV. An admixture of two or more grade was observed in 70% of our cases. The highest grade was assigned to the tumour in these cases.

When the grading was converted to two – tier system i.e., low grade (Fuhrman's grade I & II) and high grade (Fuhrman's grade III & IV) tumors, the patients were better segregated. In this scheme, 37.21% were classified under low grade category and 62.79% were classified under high grade category.

The relation between Fuhrman's nuclear grade and size of the tumour is shown in table 8. It can be seen that the mean size increases with grade.

Younger patients and those with smaller tumours tended to have lower grade tumours when compared with older patients and those with larger tumours. This association is corroborated by many other studies.

The papillary RCC tumours were assigned grade according to whether they were type I or type II tumors. 62.5% were (basophilic) type I and were classified as low grade. The remaining 37.5% were (eosinophilic) type II and were classified as high grade. There was typically sharp circumscription of the tumour from the normal tissue. All cases had tubulopapillary architecture and two of them also had cystic areas. Necrosis, foamy histiocytes in the papillary cores and inflammatory cells were seen in varying proportions.

Most of the chromophobe RCC had cells with irregular raisinoid nuclei with features of grade II. Some of them had prominent nuclei at low power examination and with features of grade III. However nuclear grading has not been recommended in chromophobe RCC.

Five cases (10.42%) of clear cell RCC had sarcomatoid areas. These areas showed fibrosarcomatous (fascicles and herring bone), malignant fibrous histocytoma – like (storiform) and undifferentiated patterns. One of our cases had > 95% area composed of sarcomatous elements and only a focal area showed clear cells and eosinophilic cells leading to a diagnosis of clear cell RCC. Another case showed rhabdomyoblast like differentiation in the form of large cells with abundant bright eosinophilic cytoplasm. There was no sarcomatoid differentiation in other subtypes of RCC.

Holger Moch et al and John C. Cheville et al have reported sarcomatoid differentiation in 8% and 5.2% of clear cell RCC respectively.

Irrespective of the proportion of sarcomatoid elements in the tumour, these cases portend a worse prognosis[29,30]. Many tumours have conclusively proven that when matched for stage, necrosis, studies size, patients with sarcomatoid differentiation have significantly worse prognosis than those without it. Hence the presence of sarcomatoid area is accepted as an independent histologic prognostic parameter.

Analyzing for correlation of nuclear grade with the amount of histologic necrosis, 81.25% of low grade tumours had necrosis < 25% and 18.75% had necrosis 25 – 50%. In comparison, only 22.22% of high grade tumours had necrosis < 25%, 51.85% had necrosis 25 – 50% and 25.93% had >50% necrosis. Thus increasing nuclear grade positively correlated with the amount of histologic necrosis.

In the chi square test analysis, this difference was found to be highly significant ($\chi^2 = 16.10$, D.F. = 2 and $P < 0.001$).

Some authors have found that histologic tumour necrosis was significantly associated with death from clear cell RCC and chromophobe RCC but not papillary RCC.

Invasion of the renal capsule and renal sinus veins upstages the tumour and were analysed in all cases 18.61% of clear cell RCC showed capsular invasion only, 27.91% of clear cell RCC showed vascular invasion only, whereas 41.86% clear cell RCC showed both capsular and vascular invasion and 11.62% did not have either.

These parameters were also analysed gradewise in the Fuhrmans and two tier system. From these data, it was noted that there was a definite propensity for invasion with increasing grade.

All high grade tumours showed either capsular or vascular invasion, with 66.67% of them showing both. In the low grade tumours, 68.75% shoed either capsular or vascular invasion and the remainder did not show any invasion.

The significance level of the difference between proportion of low and high grade tumours showing capsular invasion was calculated using Chi – square test. $\chi^2 = 9.11$ and $P < 0.005$. This showed that the difference was highly significant and not attributable to chance alone.

The same test was carried out for vascular invasion data and the χ^2 value was 12.56, $P < 0.001$ which again was highly significant.

The renal sinus and the veins in it are easily invaded owing to the lack of a connective tissue capsule between them and the tumour. So sinus invasion occur earlier than capsular invasion in many cases.

In our study, more tumours showed evidence of sinus vein invasion (n=30) than capsular invasion (n=26). This is in line with the above mentioned argument regarding invasion.

Some authors believe that grade III and grade IV tumors do not have sufficient difference in patients outcome to justify their separation into two categories. They advocate using only two grades instead of four. We analysed

grade III and IV tumours for differences in prognostic parameters such as histologic tumour necrosis, capsular and vascular invasion using χ^2 test.

When relation with necrosis was tested, a χ^2 value of 2 with two degree of freedom and $P > 0.1$ was obtained, which showed that there was no significant difference.

For association with capsular invasion, a χ^2 value of 0.01 and $P > 0.5$ was obtained. Similarly, vascular invasion data yielded χ^2 value of 0.46 and $P > 0.4$ which also discounted any significant difference among grade III and grade IV tumours.

Among the eight cases of papillary RCC in our series, two showed invasion of the capsule but none of them had vascular invasion.

All the chromophobe RCC were well circumscribed lesions and none of them showed evidence of invasion either grossly or microscopically. Out of the 7 cases, 5 had typical morphology and 2 were eosinophilic variants. Chromophobe RCC, especially the eosinophilic variant can be distinguished from oncocytoma by the use of Hale's colloidal iron stain. Strong diffuse and reticular positivity in cytoplasm was seen conforming to the diagnosis of chromophobe RCC. The microvesicles, which are the cause for this appearance on Hale's stain, are an integral and unique morphologic feature of this tumour. Electron microsopy can also be of use in demonstrating these microvesicles.

The exact nature of these microvesicles is not known. Some authors propose a mitochondrial origin but there is no direct evidence to that effect.

Bonsib and Lager, in a study of 5 chromophobe RCC, encountered a rare transitional form in which budding of a vesicle appeared to occur from the outer mitochondrial membrane. They did not endorse the concept of a mitochondrial origin because of the rarity of such findings.

There were 12 cases of TCC in our study with a male – female ratio of 5 : 1. The peak incidence was seen in the seventh decade, but unlike RCC, a number of cases occurred in the younger age group also. All the tumours were centred at the renal pelvis. Three cases exhibited multifocality and six cases showed ureteric invasion. All of them had invaded the renal parenchyma as well. In general, TCC had more friable and necrotic areas than did RCC. When the grading system of bladder TCC was applied to these cases, all of them were seen to have grade III features.

In the benign tumours category, we had 3 cases of angiomyolipoma and 1 case of hemangioma. All of them had pre operatively been classified as malignant tumours on the basis of clinical and radiological data. Even the gross features gave an impression of renal cell carcinoma and only histopathological examination revealed the true nature of these lesions.

Fig.1, Clear cell RCC – External appearance

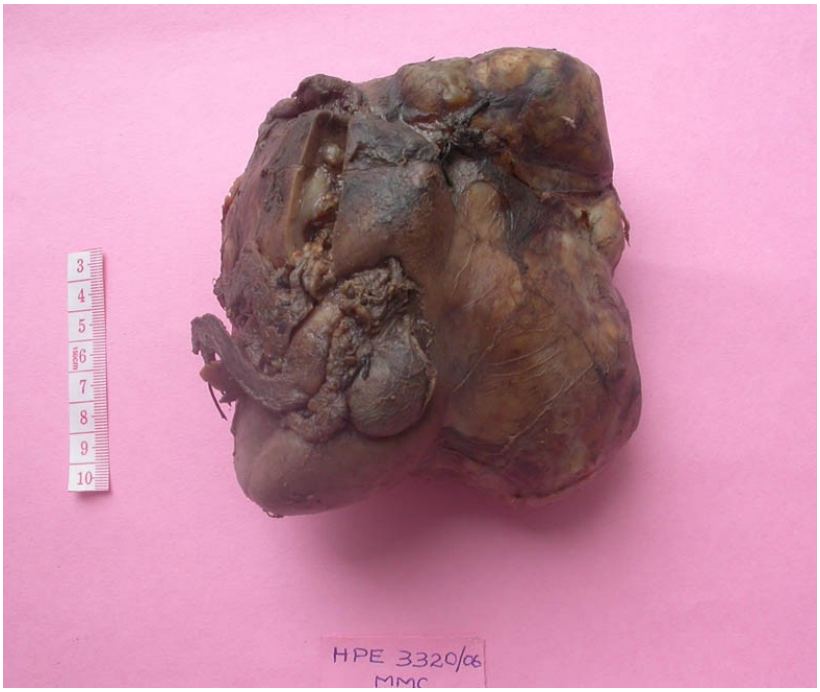


Fig.2, Clear Cell RCC
External appearance after stripping the capsule

Fig.3, Clear cell RCC showing solid and cystic areas. Normal kidney at upper and lower poles

Fig.4, Large cystic and solid areas in clear cell RCC

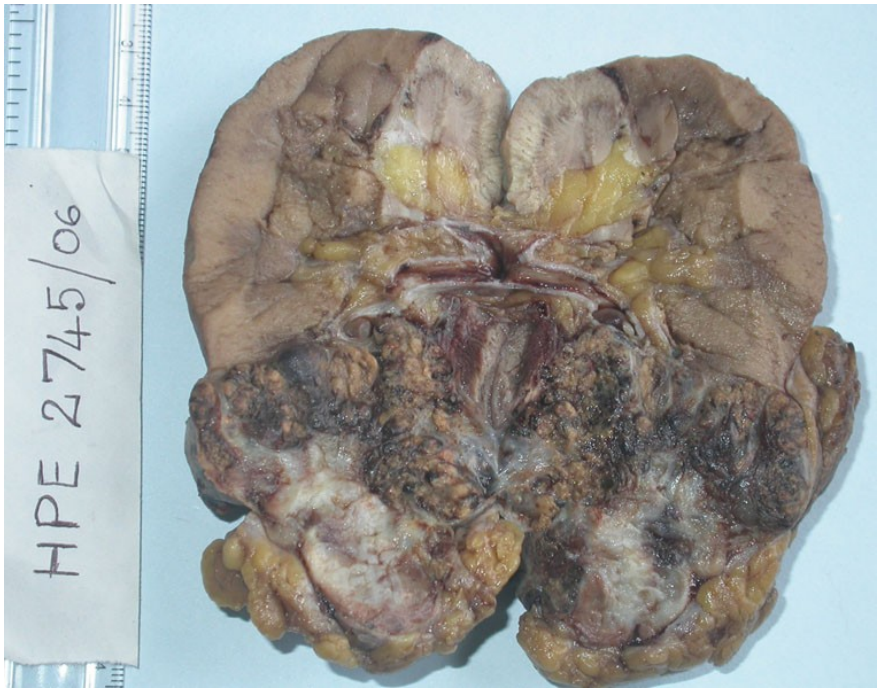


Fig.5, Clear Cell RCC – Cut Surface

Fig.6, Clear Cell RCC – Cut Surface
Normal kidney at lower pole only

Fig.7, Chromophobe RCC
Brown coloured mass occupying almost entire kidney

Fig.8, Papillary RCC
The tumour extensively replaced the kidney parenchyma

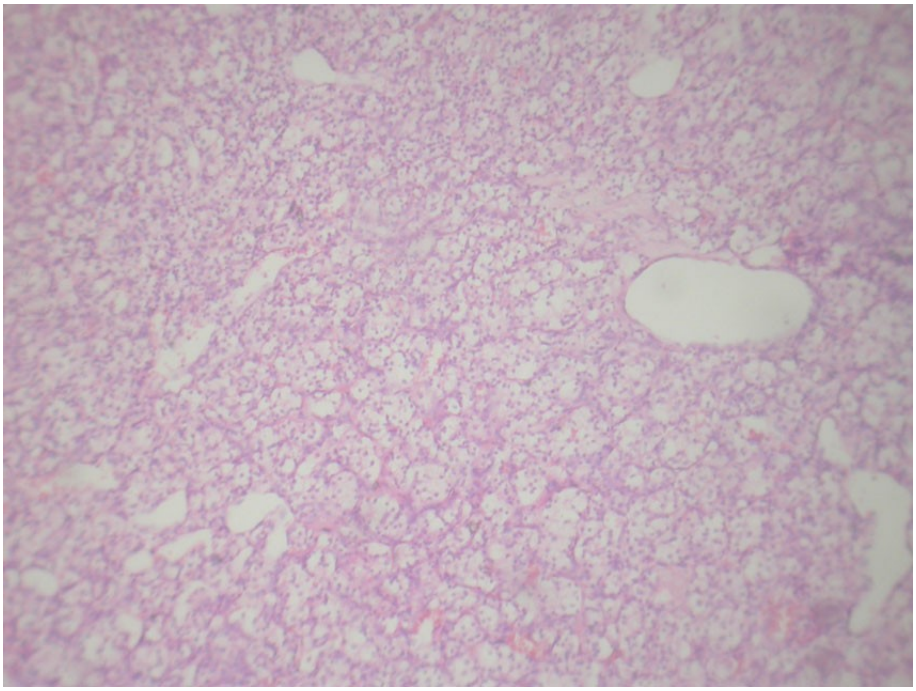


Fig.9, Clear cell RCC – Fuhrman's nuclear grade I (Low Power)

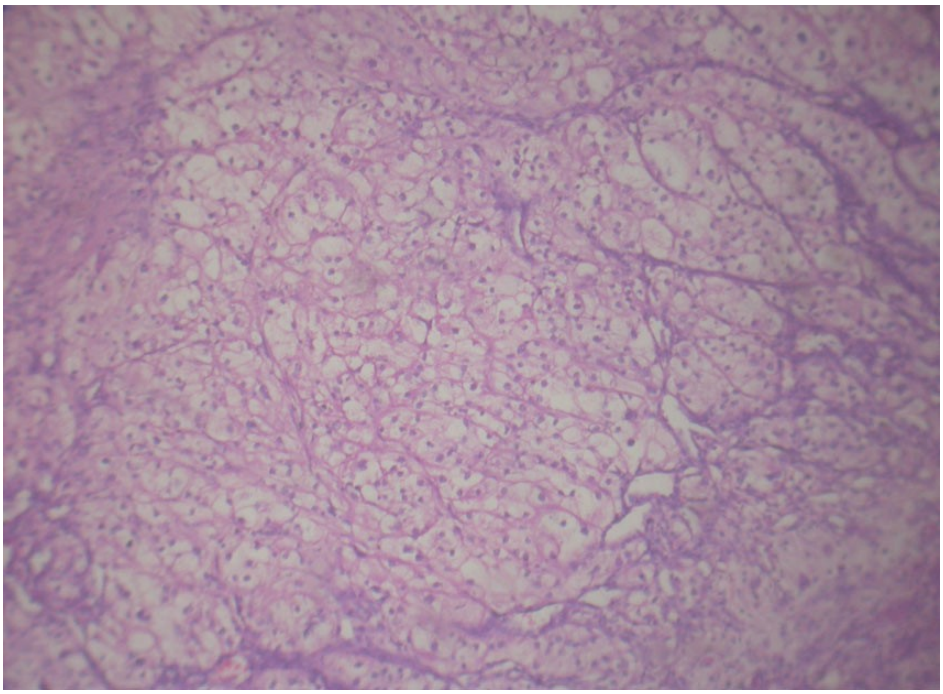


Fig.10, Clear cell RCC – Fuhrman's nuclear grade II (Low Power)

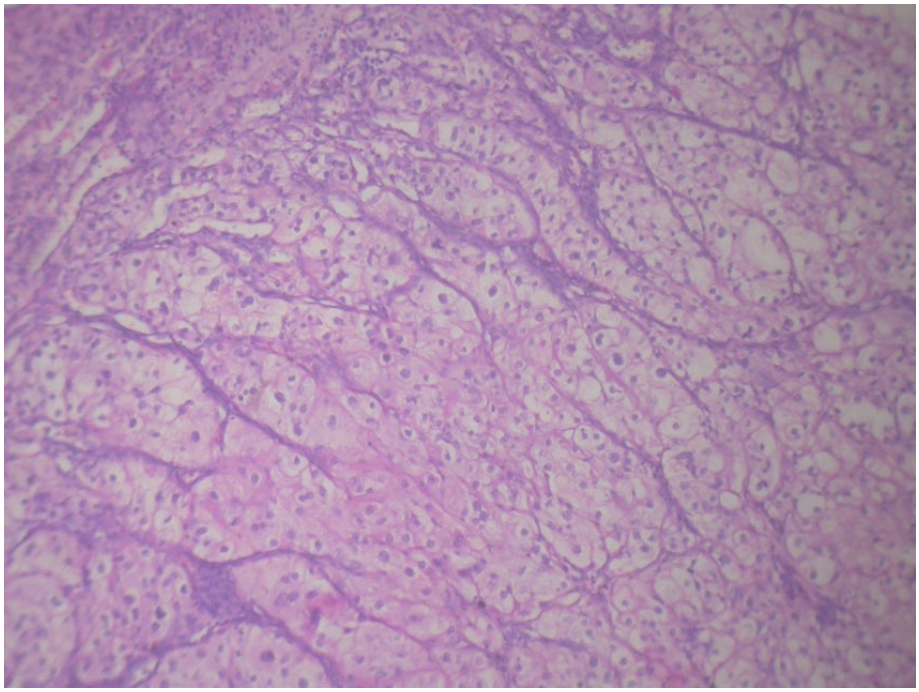


Fig.11, Clear cell RCC – Fuhrman's nuclear grade III (Low Power)
Arborising vasculature is also evident

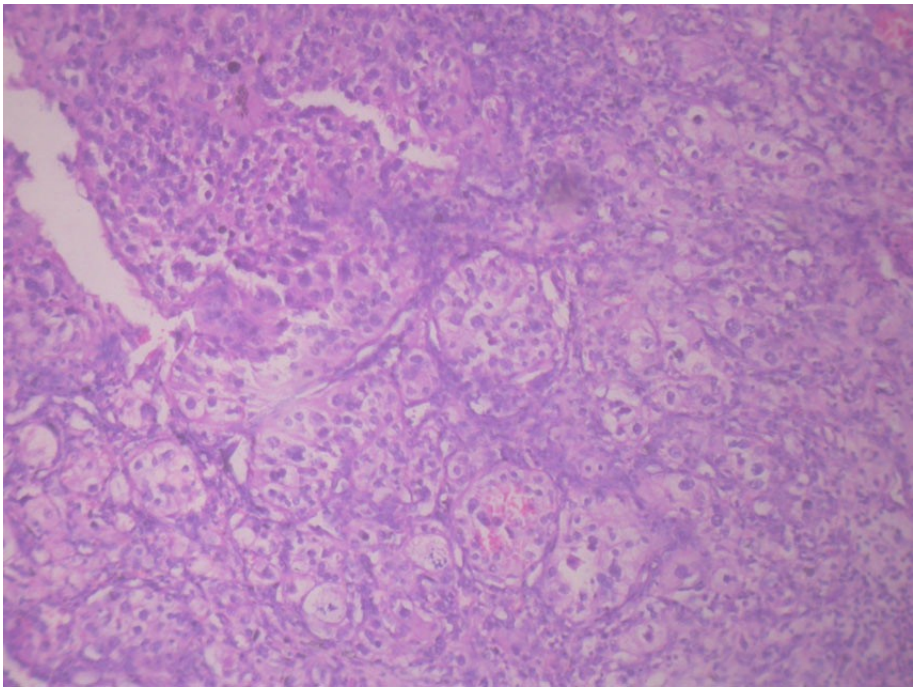


Fig.12, Clear cell RCC – Fuhrman's nuclear grade IV (Low Power)
Few mitotic figures seen

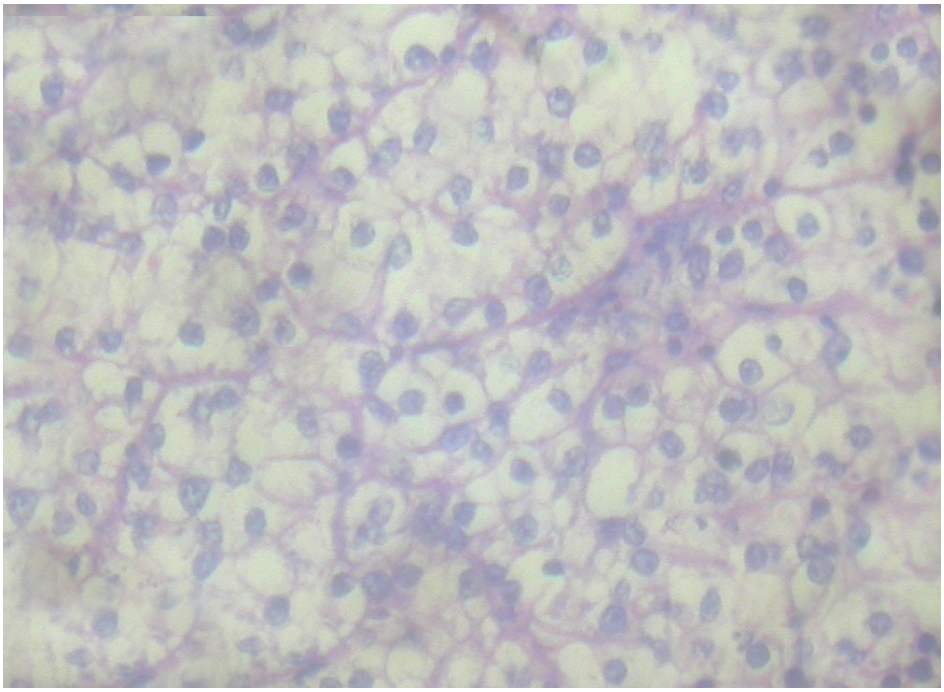


Fig.13, The cells of clear cell RCC – polygonal shaped with well defined cell borders (High Power)

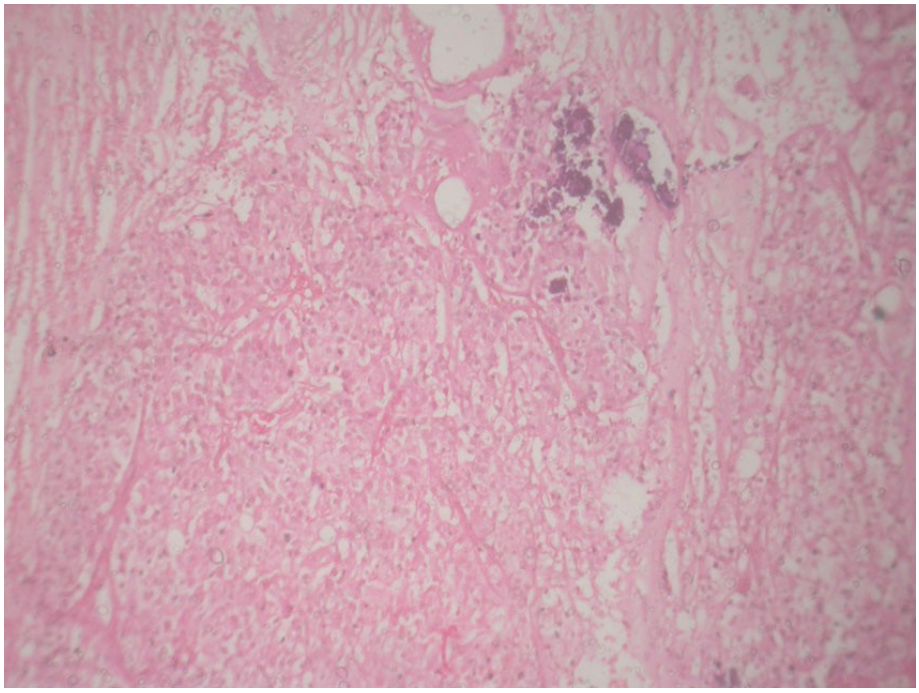


Fig.14, Clear cell RCC with focus of calcification (Low Power)

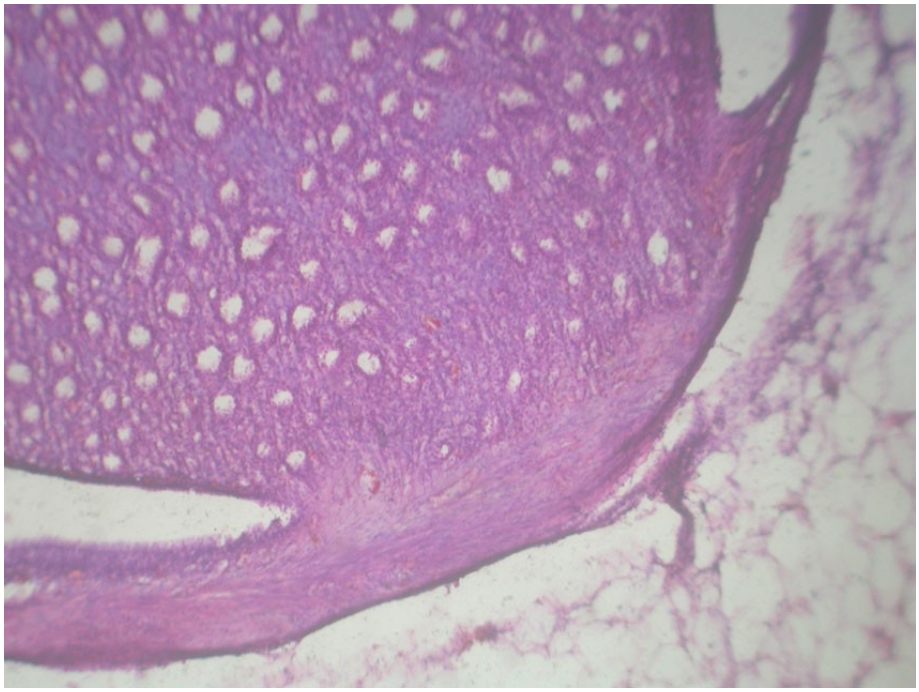
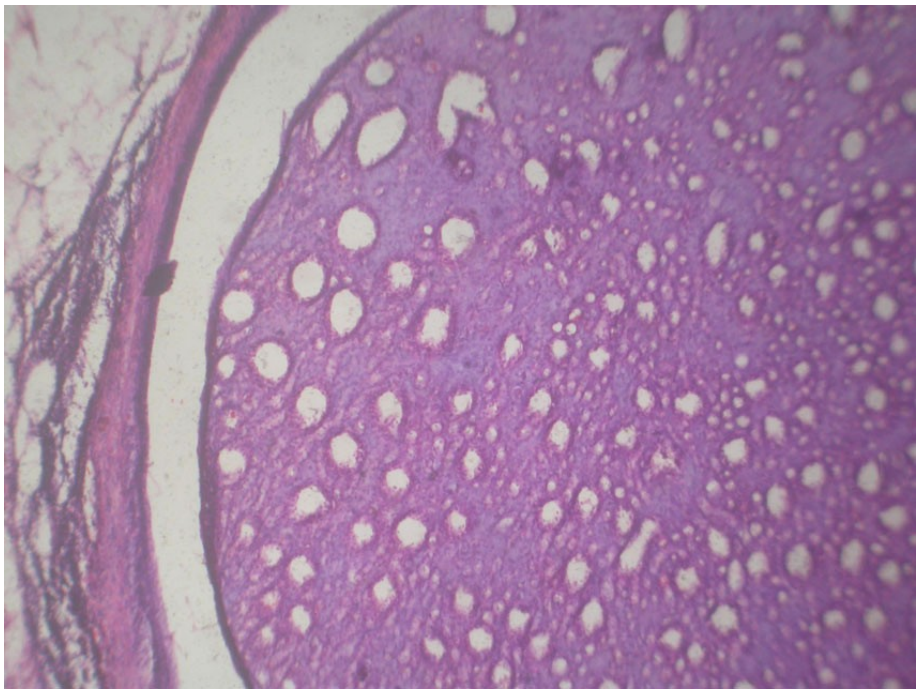


Fig.15, 16 Mesh thrombus in a sinus vein (Scanner View)



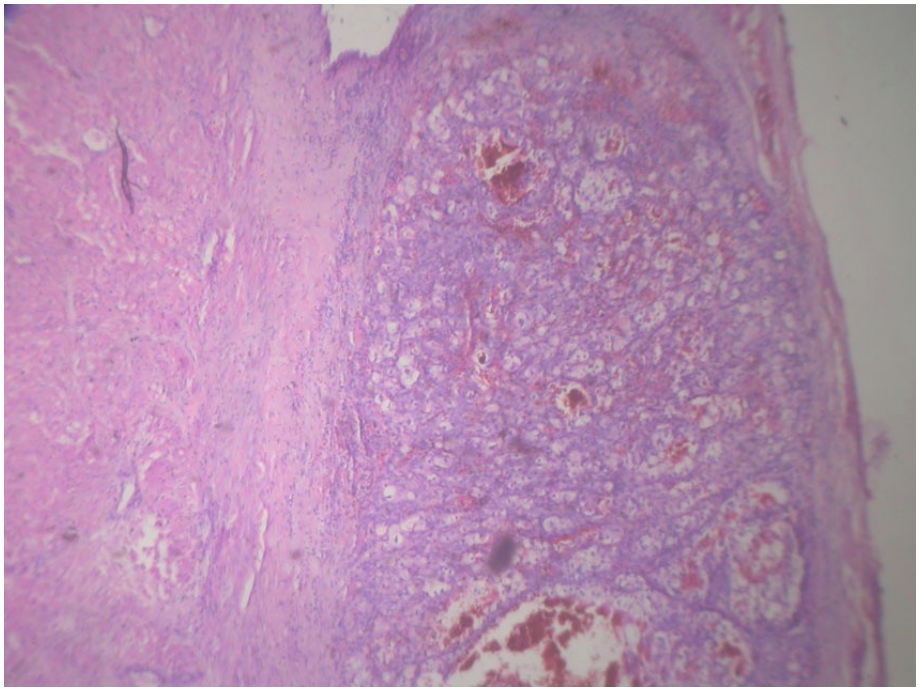


Fig.17, Tumour thrombus in clear cell RCC (Low Power)

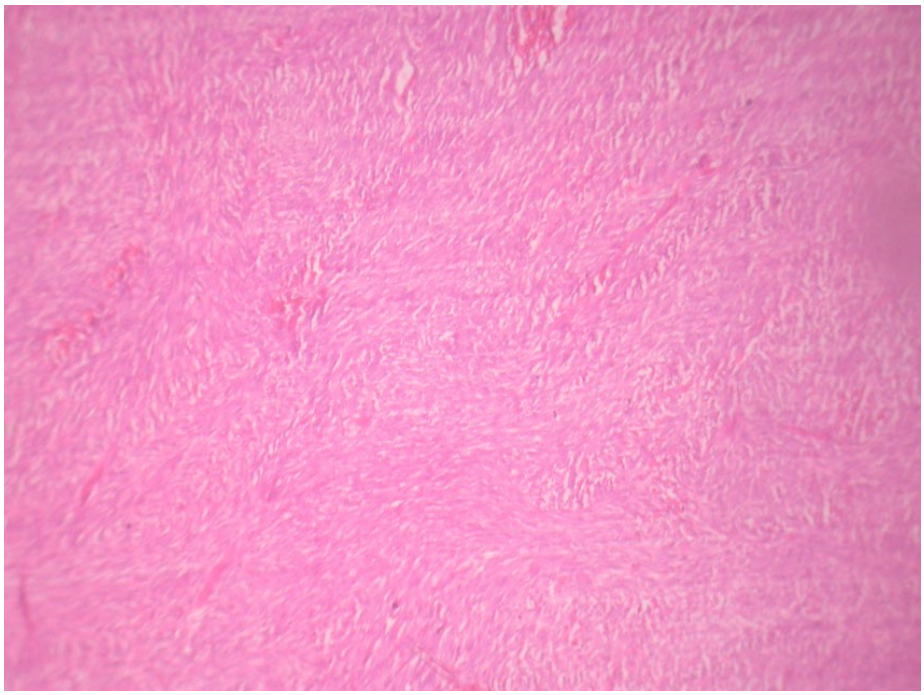


Fig.18, Sarcomatoid pattern in clear cell RCC (low power)

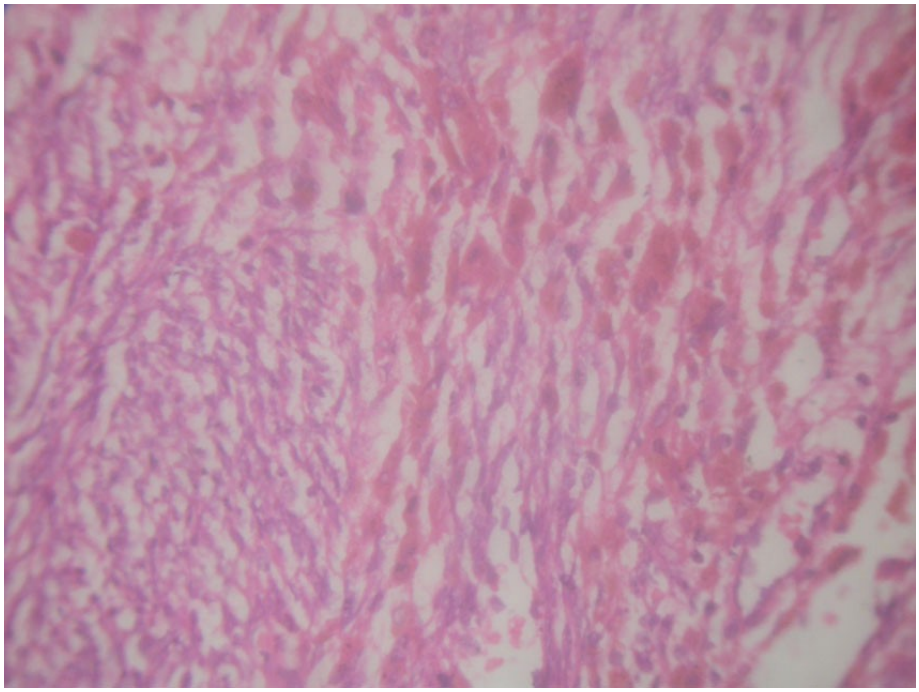


Fig.19, Rhabdomyoblast – like differentiation in sarcomatoid area (High Power)

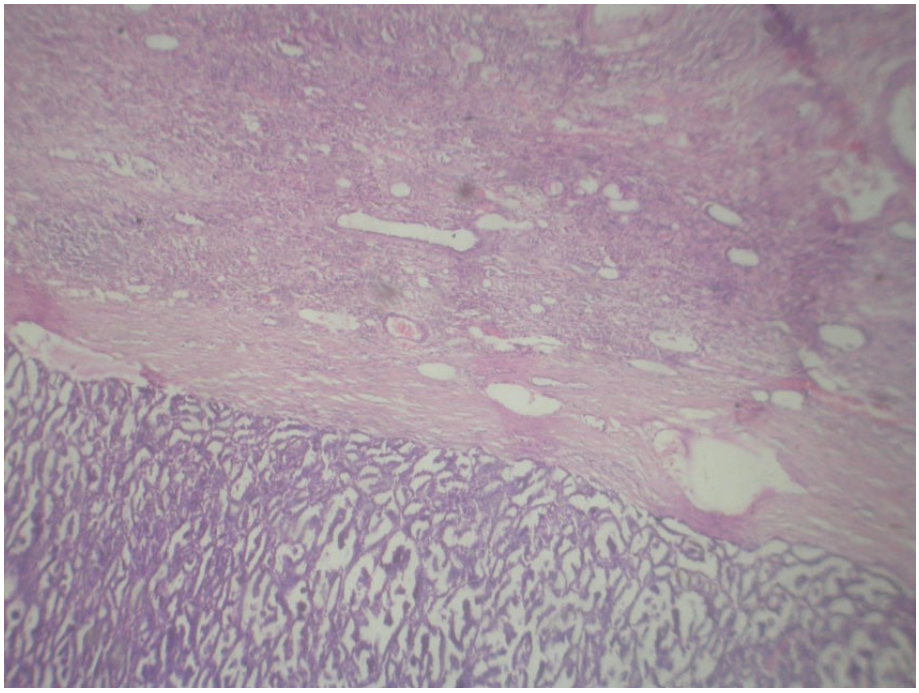


Fig.20, Encapsulation and sharp circumscription in papillary RCC (Low Power)

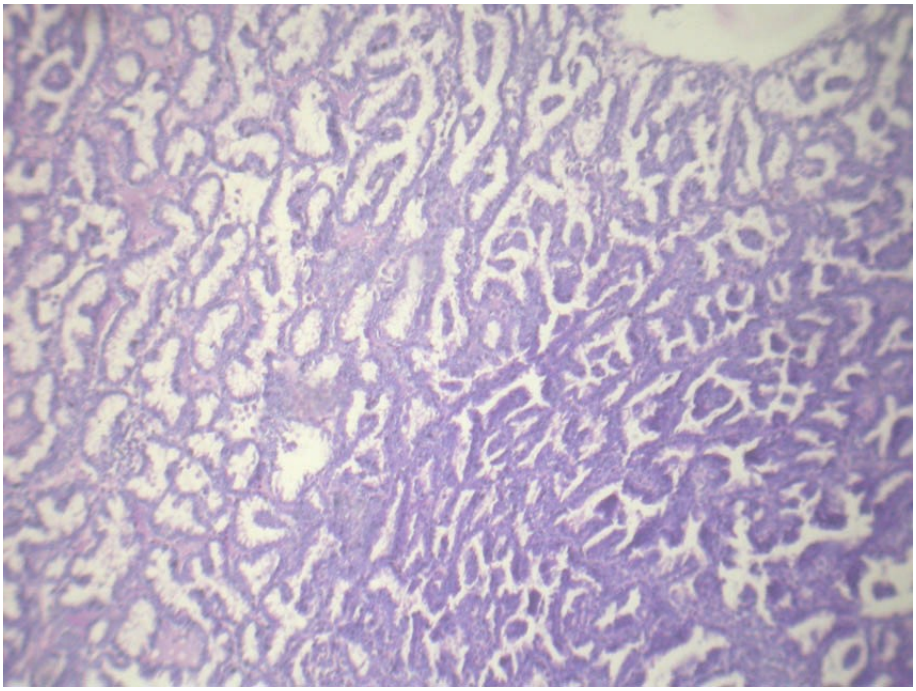


Fig.21, Tubulopapillary Areas in Type 1 Papillary RCC (Low Power)

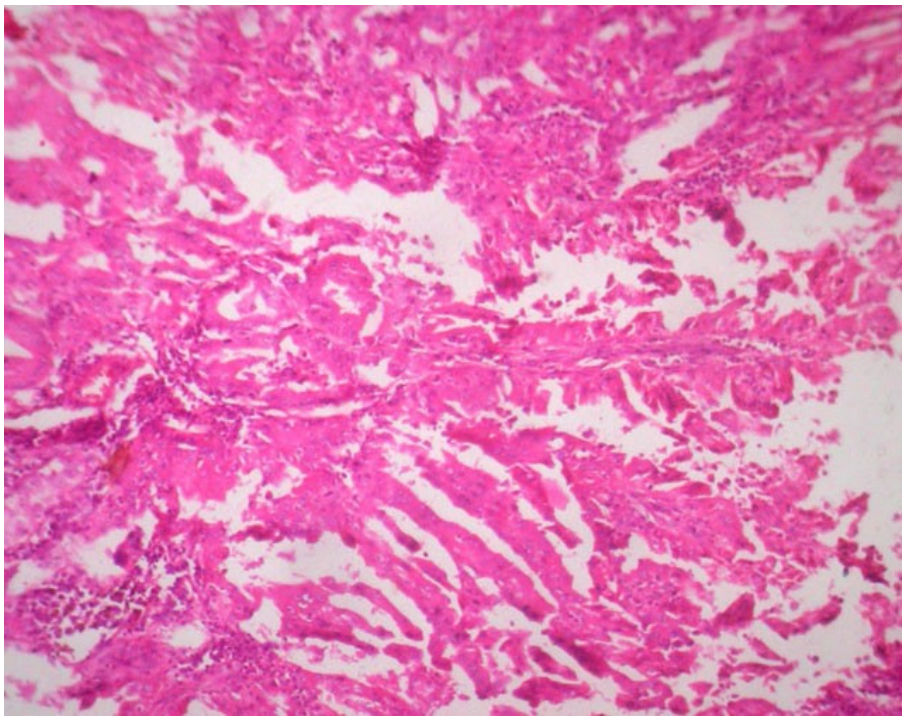


Fig.22, Type II Papillary RCC – Eosinophilic Cells (Low Power)

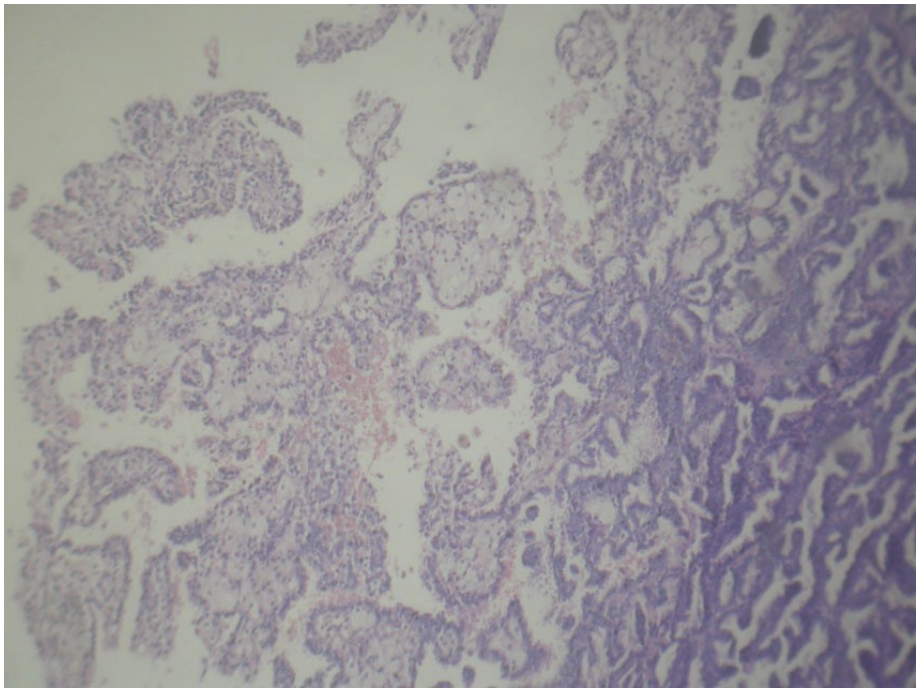


Fig.23, Papillary cores distended with foamy histiocytes (Low Power)

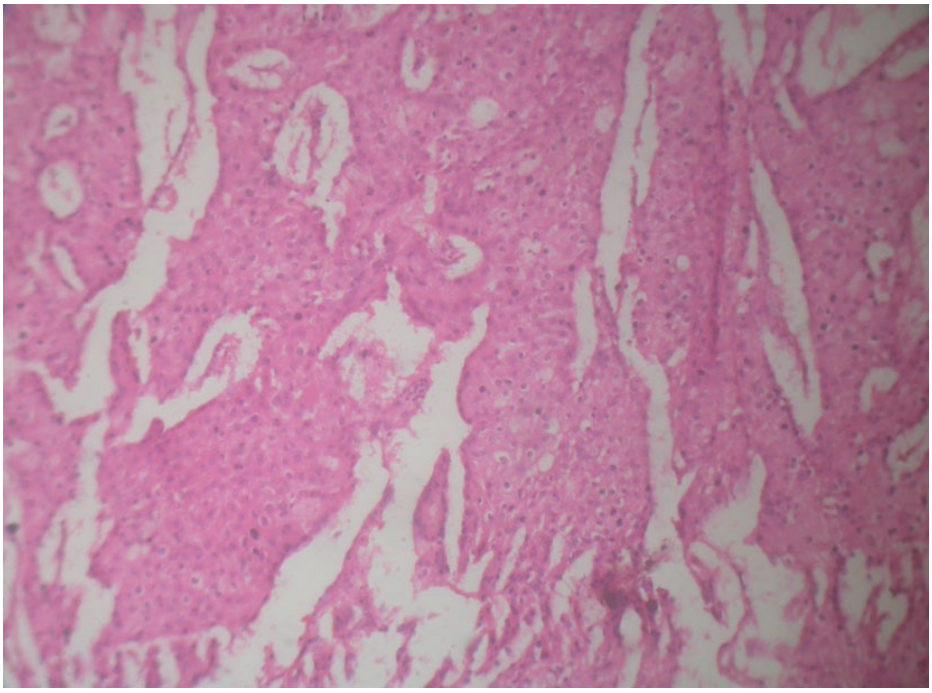


Fig.24, Chromophobe RCC
Typical Cells with Perinuclear Halo (Low Power)

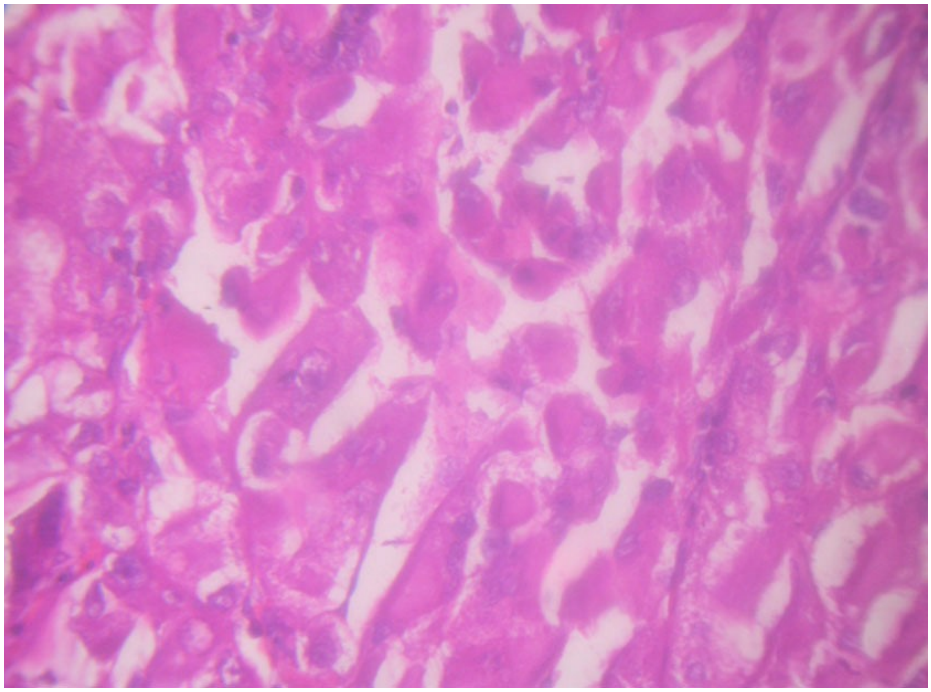


Fig.25, Chromophobe RCC – Eosinophilic cells (High Power)

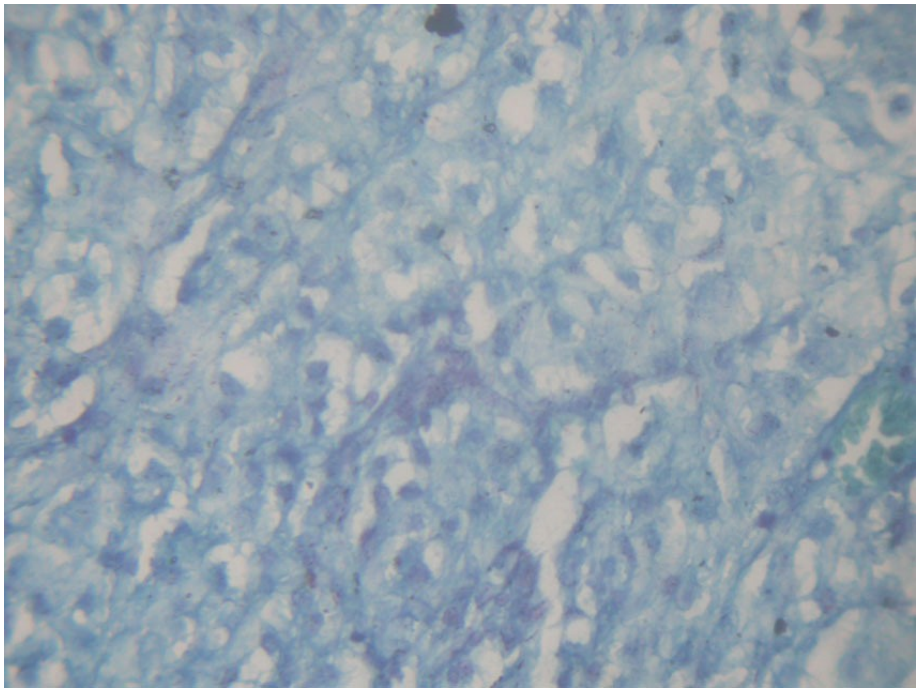


Fig.26, Chromophobe RCC Hale's Colloidal Iron Stain Diffuse and Reticular Positivity (High Power)

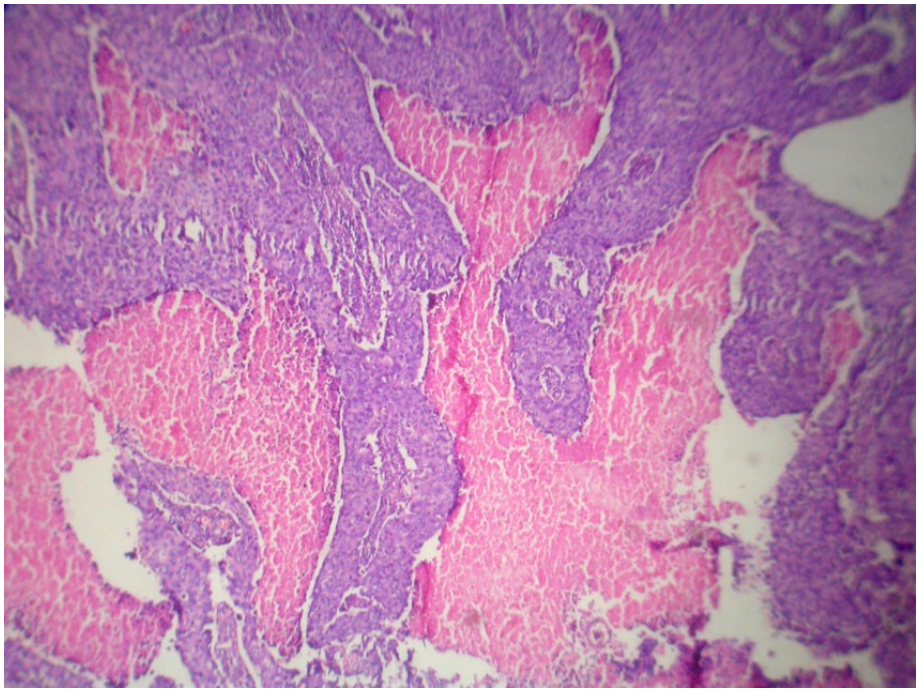


Fig.27, TCC with large areas of necrosis (Low Power)

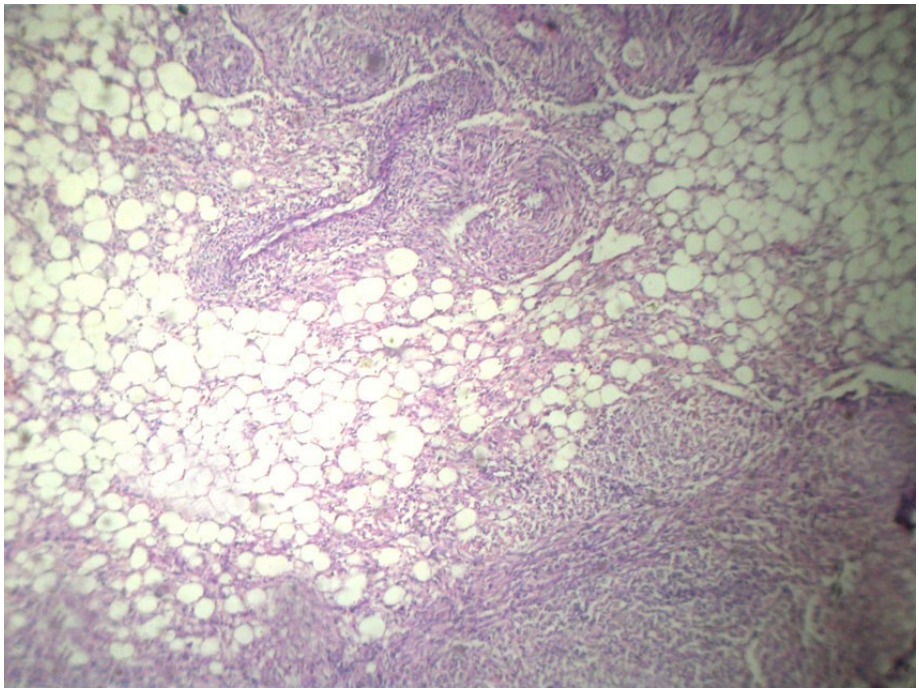


Fig.28, Angiomyolipoma
Admixture of Fat, Smooth muscle, Blood Vessel (Low Power)

SUMMARY AND CONCLUSION

1. The incidence of RCC appears to be on the rise in our study population.
2. The age of the patient and size of the tumour show good correlation with histological grade.
3. Renal sinus invasion appears to precede the capsular invasion.
4. The amount of histologic tumour necrosis shows significant association with other prognostic parameters.

Our knowledge of the biology of renal tumors has come a long way from the time when they were classified based on gross morphology alone to the present day when a combined multimodal approach using conventional histology, special histochemical stains, immunohistology, molecular biology and cytogenetics is used to classify these tumors. Nevertheless, the time – tested. Hematoxylin and Eosin section is still sufficient to diagnose a majority of the lesions and the information gained from these sections have overriding mandate over the data obtained from other ancillary techniques.

In our study, we had attempted to define the histomorphological profile of adult renal tumors among patients treated at our Institution. The results in general were comparable to those reported from other large series studies. The important histologic prognostic parameters were nuclear grade, presence of sarcomatoid component, amount of necrosis and should be consistently documented in all cases of RCC to stratify patients by prognosis. These prognostic parameters differed by histological subtype. A

significant proportion of RCC, apparently renal – limited, had entered renal sinus fat and sinus veins which could indicate an important portal for metastasis. Hence handling of renal carcinoma specimens in the gross room must also focus on the renal sinus. The grading of RCC as low and high grades, resulted in the division of tumours into two well defined categories which had significant differences in their association with known prognostic parameters.

The study of various pathological features of renal tumours and their patterns of invasion helps in unraveling the natural history of these lesions. Without this knowledge of tumour behaviour, it would be difficult to decide on conservative treatment options for small renal – limited tumours. Prospective studies with adequate patient follow up data are required for this purpose. The importance of subtyping may further increase as advanced treatment modalities like tumor vaccines,immunotherapy and gene therapy[31] come into routine oncologic practice and management becomes individualised to each patient.

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MASTER CHART

S. NO.	HPE NO	AGE	SEX	LATERALITY	PROCEDURE	DIAGNOSIS	GRADE
1.	219/ 03	75yrs	M	Left	Radical nephrectomy	TCC	III
2.	567/ 03	40 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	II
3.	893/ 03	50 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
4.	1557/ 03	48 yrs	F	Left	Consultation slide	Clear Cell RCC	IV
5.	1828/ 03	65 yrs	M	Right	Imaging guided Biopsy	Clear Cell RCC	Not graded
6.	2086/ 03	62 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	I
7.	2877/ 03	60 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
8.	3018/ 03	56 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	II
9.	3286/ 03	58 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
10.	3743/ 03	22 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
11.	4025/ 03	52yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
12.	4525/ 03	60 yrs	F	Left	Imaging guided Biopsy	Clear Cell RCC	Not graded
13.	4571/ 03	60 yrs	M	Left	Radical nephrectomy	TCC	II
14.	4676/ 03	55 yrs	M	Left	Imaging guided Biopsy	Clear Cell RCC	Not graded
15.	4885/ 03	65 yrs	F	Left	Radical nephrectomy	TCC	III
16.	5271/ 03	60 yrs	M	Right	Consultation slide	Clear Cell RCC	Not graded
17.	5315/ 03	50 yrs	M	Right	Radical nephrectomy	TCC	III
18.	5468/ 03	50 yrs	F	Right	Radical nephrectomy	Angiomyolipoma	-
19.	5773/ 03	30 yrs	F	Right	Radical nephrectomy	Chromophobe RCC	Not Graded

S. NO.	HPE NO	AGE	SEX	LATERALITY	PROCEDURE	DIAGNOSIS	GRADE
20.	5927/ 03	53 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	IV
21.	6125/ 03	51 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
22.	19/ 04	65 yrs	M	Right	Radical nephrectomy	TCC	III
23.	782/ 04	40 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
24.	885/ 04	50 yrs	M	Right	Radical nephrectomy	TCC	III
25.	975/ 04	47 yrs	M	Right	Radical nephrectomy	TCC	III
26.	1282/ 04	44 yrs	F	Left	Radical nephrectomy	Chromophobe RCC	Not Graded
27.	2169/ 04	50 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
28.	2264/ 04	55 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	II
29.	2501/ 04	68 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	III
30.	2576/ 04	73 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	IV
31.	3163/ 04	30 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
32.	3376/ 04	60 yrs	M	Right	Imaging guided Biopsy	Clear Cell RCC	Not Graded
33.	3695/ 04	56 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
34.	4098/ 04	60 yrs	M	Right	Radical nephrectomy	Papillary RCC type 2	High grade
35.	4418/ 04	55 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
36.	5306/ 04	75 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	III
37.	5391/ 04	32 yrs	M	Left	Imaging guided Biopsy	TCC	III
38.	6130/ 04	65 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
39.	6269/ 04	80 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	II
40.	6484/ 04	60 yrs	M	Left	Imaging guided Biopsy	Clear Cell RCC	Not Graded

S. NO.	HPE NO	AGE	SEX	LATERALITY	PROCEDURE	DIAGNOSIS	GRADE
41.	6878/ 04	73 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	IV
42.	7073/ 04	35 yrs	M	Left	Radical nephrectomy	TCC	III
43.	7214/ 04	57 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
44.	7275/ 04	55 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	III
45.	7449/ 04	58 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
46.	7492/ 04	62 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
47.	139/ 05	55 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	IV
48.	254/ 05	60 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
49.	494/ 05	48 yrs	F	Right	Radical nephrectomy	Papillary RCC type 1	I
50.	805/ 05	70 yrs	M	Left	Radical nephrectomy	Papillary RCC type 2	II
51.	808/ 05	48 yrs	M	Right	Radical nephrectomy	Angiomyolipoma	-
52.	1224/ 05	38 yrs	M	Right	Radical nephrectomy	Chromophobe RCC	Not graded
53.	1674/05	64 yrs	M	Left	Radical nephrectomy	TCC	III
54.	2320/ 05	39 yrs	M	Left	Radical nephrectomy	Papillary RCC type 2	II
55.	3017/ 05	45 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
56.	3388/ 05	45 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
57.	4332/ 05	60 yrs	F	Right	Radical nephrectomy	TCC	III
58.	4357/ 05	55 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
59.	4358/ 05	65 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	IV
60.	4508/ 05	24 yrs	F	Right	Radical nephrectomy	Clear Cell RCC	III
61.	4701/ 05	33 yrs	M	Right	Radical nephrectomy	TCC	III

S. NO.	HPE NO	AGE	SEX	LATERALITY	PROCEDURE	DIAGNOSIS	GRADE

62.	5490/ 05	60 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
63.	6228/ 05	22 yrs	F	Left	Radical nephrectomy	Angiomyolipoma	-
64.	6464/ 05	32 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	II
65.	6493/ 05	65 yrs	M	Left	Imaging guided biopsy	Papillary RCC type 1	I
66.	16/ 06	66 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	II
67.	68/ 06	45 yrs	F	Left	Radical nephrectomy	Clear Cell RCC	II
68.	468/ 06	62 yrs	F	Right	Radical nephrectomy	Clear Cell RCC	II
69.	562/ 06	47 yrs	M	Left	Radical nephrectomy	Chromophobe RCC	Not graded
70.	906/ 06	45 yrs	F	Left	Radical nephrectomy	Chromophobe RCC	Not graded
71.	919/ 06	35 yrs	F	Right	Radical nephrectomy	Papillary RCC type 1	I
72.	1445/ 06	45 yrs	F	Right	Radical nephrectomy	Hemangisma	-
73.	2107/ 06	65 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	III
74.	2443/ 06	50 yrs	F	Right	Radical nephrectomy	Papillary RCC type 1	I
75.	2745/ 06	50 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	II
76.	3115/ 06	65 yrs	M	Right	Radical nephrectomy	Clear Cell RCC	II
77.	3320/ 06	61 yrs	M	Left	Radical nephrectomy	Clear Cell RCC	III
78.	3748/ 06	50 yrs	M	Left	Radical nephrectomy	Chromophobe RCC	Not graded
79.	3835/ 06	50 yrs	M	Right	Radical nephrectomy	Papillary RCC type 1	I